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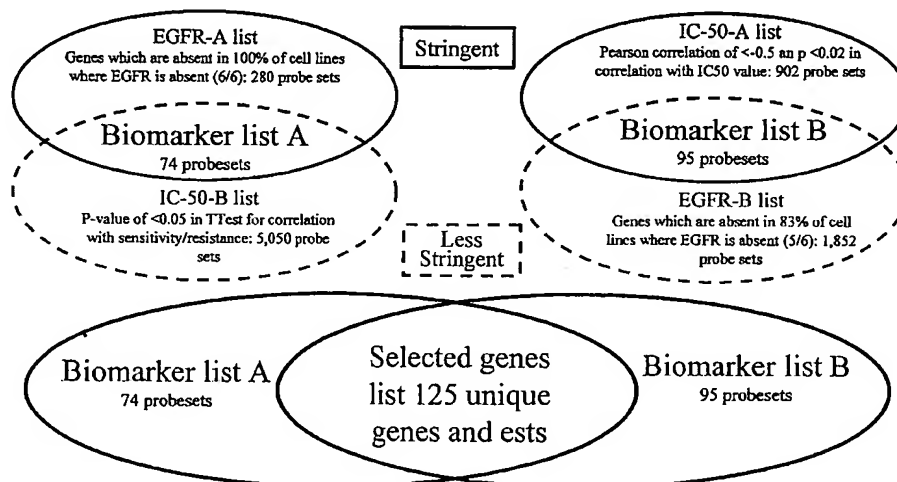
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[Continued on next page]

(54) Title: **BIOMARKERS AND METHODS FOR DETERMINING SENSITIVITY TO EPIDERMAL GROWTH FACTOR RECEPTOR MODULATORS**



(57) Abstract: EGFR biomarkers useful in a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises (a) exposing the mammal to the EGFR modulator and (b) measuring in the mammal level of at least one biomarker, wherein a difference in the level in at least one biomarker measured in (b) compared to the level of the biomarker in a mammal that has not been exposed to the EGFR modulator indicates that the mammal will respond therapeutically to the method of treating cancer.

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BIOMARKERS AND METHODS FOR DETERMINING SENSITIVITY TO EPIDERMAL GROWTH FACTOR RECEPTOR MODULATORS

FIELD OF THE INVENTION

The present invention relates generally to the field of pharmacogenomics, and more specifically to methods and procedures to determine sensitivity in patients to allow the development of individualized genetic profiles which aid in treating diseases and disorders based on patient response at a molecular level.

BACKGROUND OF THE INVENTION:

Cancer is a disease with extensive histoclinical heterogeneity. Although conventional histological and clinical features have been correlated to prognosis, the same apparent prognostic type of tumors varies widely in its responsiveness to therapy and consequent survival of the patient.

New prognostic and predictive markers, which would facilitate an individualization of therapy for each patient, are needed to accurately predict patient response to treatments, such as small molecule or biological molecule drugs, in the clinic. The problem may be solved by the identification of new parameters that could better predict the patient's sensitivity to treatment. The classification of patient samples is a crucial aspect of cancer diagnosis and treatment. The association of a patient's response to a treatment with molecular and genetic markers can open up new opportunities for treatment development in non-responding patients, or distinguish a treatment's indication among other treatment choices because of higher confidence in the efficacy. Further, the pre-selection of patients who are likely to respond well to a medicine, drug, or combination therapy may reduce the number of patients needed in a clinical study or accelerate the time needed to complete a clinical development program (M. Cockett et al., 2000, *Current Opinion in Biotechnology*, 11:602-609).

The ability to predict drug sensitivity in patients is particularly challenging because drug responses reflect not only properties intrinsic to the target cells, but also a host's metabolic properties. Efforts to use genetic information to predict drug sensitivity have primarily focused on individual genes that have broad effects, such as the multidrug resistance genes, *mdr1* and *mrp1* (P. Sonneveld, 2000, *J. Intern. Med.*, 247:521-534).

The development of microarray technologies for large scale characterization of gene mRNA expression pattern has made it possible to systematically search for molecular markers and to categorize cancers into distinct subgroups not evident by traditional histopathological methods (J. Khan et al., 1998, *Cancer Res.*, 58:5009-5013; A.A. Alizadeh et al., 2000, *Nature*, 403:503-511; M. Bittner et al., 2000, *Nature*, 406:536-540; J. Khan et al., 2001, *Nature Medicine*, 7(6):673-679; and T.R. Golub et al., 1999, *Science*, 286:531-537; U. Alon et al., 1999, *Proc. Natl. Acad. Sci. USA*, 96:6745-6750). Such technologies and molecular tools have made it possible to monitor the expression level of a large number of transcripts within a cell population at any given time (see, e.g., Schena et al., 1995, *Science*, 270:467-470; Lockhart et al., 1996, *Nature Biotechnology*, 14:1675-1680; Blanchard et al., 1996, *Nature Biotechnology*, 14:1649; U.S. Patent No. 5,569,588 to Ashby et al.).

Recent studies demonstrate that gene expression information generated by microarray analysis of human tumors can predict clinical outcome (L.J. van't Veer et al., 2002, *Nature*, 415:530-536; M. West et al., 2001, *Proc. Natl. Acad. Sci. USA*, 98:11462-11467; T. Sorlie et al., 2001, *Proc. Natl. Acad. Sci. USA*, 98:10869-10874; M. Shipp et al., 2002, *Nature Medicine*, 8(1):68-74). These findings bring hope that cancer treatment will be vastly improved by better predicting the response of individual tumors to therapy.

Needed are new and alternative methods and procedures to determine drug sensitivity in patients to allow the development of individualized genetic profiles which are necessary to treat diseases and disorders based on patient response at a molecular level.

SUMMARY OF THE INVENTION:

The invention provides methods and procedures for determining patient sensitivity to one or more Epidermal Growth Factor Receptor (EGFR) modulators. The invention also provides methods of determining or predicting whether an individual requiring therapy for a disease state such as cancer will or will not respond to treatment, prior to administration of the treatment, wherein the treatment comprises one or more EGFR modulators. The one or more EGFR modulators are compounds that can be selected from, for example, one or more EGFR specific ligands, one or

more small molecule EGFR inhibitors, or one or more EGFR binding monoclonal antibodies.

In one aspect, the invention provides a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises: (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4; (b) exposing the mammal to the EGFR modulator; (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker, wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

As used herein, respond therapeutically refers to the alleviation or abrogation of the cancer. This means that the life expectancy of an individual affected with the cancer will be increased or that one or more of the symptoms of the cancer will be reduced or ameliorated. The term encompasses a reduction in cancerous cell growth or tumor volume. Whether a mammal responds therapeutically can be measured by many methods well known in the art, such as PET imaging.

The at least one biomarker can also be selected from the biomarkers of Table 5. The mammal can be, for example, a human, rat, mouse, dog rabbit, pig sheep, cow, horse, cat, primate, or monkey.

The method of the invention can be, for example, an in vitro method and wherein the at least one biomarker is measured in at least one mammalian biological sample from the mammal. The biological sample can comprise, for example, at least one of whole fresh blood, peripheral blood mononuclear cells, frozen whole blood, fresh plasma, frozen plasma, urine, saliva, skin, hair follicle, or tumor tissue.

In another aspect, the invention provides a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises: (a) exposing the mammal to the EGFR modulator; (b) following the exposing of step (a), measuring in the mammal the level of the at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of the at least one biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been

exposed to said EGFR modulator, indicates that the mammal will respond therapeutically to said method of treating cancer.

In yet another aspect, the invention provides a method for testing or predicting whether a mammal will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises: (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4; (b) exposing the mammal to the EGFR modulator; (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker, wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

In another aspect, the invention provides a method for determining whether a compound inhibits EGFR activity in a mammal, comprising: (a) exposing the mammal to the compound; and (b) following the exposing of step (a), measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of said biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said compound, indicates that the compound inhibits EGFR activity in the mammal.

In yet another aspect, the invention provides a method for determining whether a mammal has been exposed to a compound that inhibits EGFR activity, comprising (a) exposing the mammal to the compound; and (b) following the exposing of step (a), measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of said biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said compound, indicates that the mammal has been exposed to a compound that inhibits EGFR activity.

In another aspect, the invention provides a method for determining whether a mammal is responding to a compound that inhibits EGFR activity, comprising (a) exposing the mammal to the compound; and (b) following the exposing of step (a), measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of said biomarker measured

in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said compound, indicates that the mammal is responding to the compound that inhibits EGFR activity.

As used herein, "responding" encompasses responding by way of a biological and cellular response, as well as a clinical response (such as improved symptoms, a therapeutic effect, or an adverse event), in a mammal

The invention also provides an isolated biomarker selected from the biomarkers of Table 4. The biomarkers of the invention comprise sequences selected from the nucleotide and amino acid sequences provided in Table 4 and the Sequence Listing, as well as fragments and variants thereof.

The invention also provides a biomarker set comprising two or more biomarkers selected from the biomarkers of Table 4.

The invention also provides kits for determining or predicting whether a patient would be susceptible or resistant to a treatment that comprises one or more EGFR modulators. The patient may have a cancer or tumor such as, for example, a colon cancer or tumor.

In one aspect, the kit comprises a suitable container that comprises one or more specialized microarrays of the invention, one or more EGFR modulators for use in testing cells from patient tissue specimens or patient samples, and instructions for use. The kit may further comprise reagents or materials for monitoring the expression of a biomarker set at the level of mRNA or protein.

In another aspect, the invention provides a kit comprising two or more biomarkers selected from the biomarkers of Table 4.

In yet another aspect, the invention provides a kit comprising at least one of an antibody and a nucleic acid for detecting the presence of at least one of the biomarkers selected from the biomarkers of Table 4. In one aspect, the kit further comprises instructions for determining whether or not a mammal will respond therapeutically to a method of treating cancer comprising administering a compound that inhibits EGFR activity. In another aspect, the instructions comprise the steps of (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, (b) exposing the mammal to the compound, (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker,

wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

The invention also provides screening assays for determining if a patient will
5 be susceptible or resistant to treatment with one or more EGFR modulators.

The invention also provides a method of monitoring the treatment of a patient having a disease treatable by one or more EGFR modulators.

The invention also provides individualized genetic profiles which are necessary to treat diseases and disorders based on patient response at a molecular
10 level.

The invention also provides specialized microarrays, e.g., oligonucleotide microarrays or cDNA microarrays, comprising one or more biomarkers having expression profiles that correlate with either sensitivity or resistance to one or more EGFR modulators.

15 The invention also provides antibodies, including polyclonal or monoclonal, directed against one or more biomarkers of the invention.

The invention will be better understood upon a reading of the detailed description of the invention when considered in connection with the accompanying figures.

20

BRIEF DESCRIPTION OF THE FIGURES:

FIG. 1 illustrates a EGFR biomarker identification and prioritization strategy.

FIG. 2A illustrates the RT-PCR results for EGFR in thirty one colon cancer cell lines to identify cell lines which do not have significant mRNA expression of
25 EGFR.

FIG. 2B illustrates the IC₅₀ profile for twenty two colon cancer cell lines with an EGFR inhibitor compound, and determination of sensitive and resistant cell lines.

DETAILED DESCRIPTION OF THE INVENTION:

The invention provides biomarkers that respond to the modulation of a specific signal transduction pathway and also correlate with EGFR modulator sensitivity or resistance. These biomarkers can be employed for predicting response to one or more EGFR modulators. In one aspect, the biomarkers of the invention are those provided in Table 4 and the Sequence Listing, including both polynucleotide and polypeptide sequences.

The biomarkers were determined by an *in vitro* assay employing microarray technology to monitor simultaneously the expression pattern of thousands of discrete genes in untreated cells, whose response to the modulation of a signal transduction pathway, in particular the EGFR pathway, was tested on untreated cells whose sensitivity to EGFR modulators was tested. The biomarkers have expression levels in the cells that are dependent on the activity of the EGFR signal transduction pathway and that are also highly correlated with EGFR modulator sensitivity exhibited by the cells. Biomarkers serve as useful molecular tools for predicting a response to EGFR modulators, preferably biological molecules, small molecules, and the like that affect EGFR kinase activity via direct or indirect inhibition or antagonism of EGFR kinase function or activity.

EGFR MODULATORS

As used herein, the term "EGFR modulator" is intended to mean a compound or drug that is a biological molecule or a small molecule that directly or indirectly modulates EGFR activity or the EGFR signal transduction pathway. Thus, compounds or drugs as used herein is intended to include both small molecules and biological molecules. Direct or indirect modulation includes activation or inhibition of EGFR activity or the EGFR signal transduction pathway. In one aspect, inhibition refers to inhibition of the binding of EGFR to an EGFR ligand such as, for example, EGF. In another aspect, inhibition refers to inhibition of the kinase activity of EGFR.

EGFR modulators include, for example, EGFR specific ligands, small molecule EGFR inhibitors, and EGFR monoclonal antibodies. In one aspect, the EGFR modulator inhibits EGFR activity and/or inhibits the EGFR signal transduction

pathway. In another aspect, the EGFR modulator is an EGFR antibody that inhibits EGFR activity and/or inhibits the EGFR signal transduction pathway.

EGFR modulators include biological molecules or small molecules.

Biological molecules include all lipids and polymers of monosaccharides, amino acids, and nucleotides having a molecular weight greater than 450. Thus, biological molecules include, for example, oligosaccharides and polysaccharides; oligopeptides, polypeptides, peptides, and proteins; and oligonucleotides and polynucleotides. Oligonucleotides and polynucleotides include, for example, DNA and RNA.

Biological molecules further include derivatives of any of the molecules described above. For example, derivatives of biological molecules include lipid and glycosylation derivatives of oligopeptides, polypeptides, peptides, and proteins.

Derivatives of biological molecules further include lipid derivatives of oligosaccharides and polysaccharides, e.g., lipopolysaccharides. Most typically, biological molecules are antibodies, or functional equivalents of antibodies.

Functional equivalents of antibodies have binding characteristics comparable to those of antibodies, and inhibit the growth of cells that express EGFR. Such functional equivalents include, for example, chimerized, humanized, and single chain antibodies as well as fragments thereof.

Functional equivalents of antibodies also include polypeptides with amino acid sequences substantially the same as the amino acid sequence of the variable or hypervariable regions of the antibodies. An amino acid sequence that is substantially the same as another sequence, but that differs from the other sequence by means of one or more substitutions, additions, and/or deletions, is considered to be an equivalent sequence. Preferably, less than 50%, more preferably less than 25%, and still more preferably less than 10%, of the number of amino acid residues in a sequence are substituted for, added to, or deleted from the protein.

The functional equivalent of an antibody is preferably a chimerized or humanized antibody. A chimerized antibody comprises the variable region of a non-human antibody and the constant region of a human antibody. A humanized antibody comprises the hypervariable region (CDRs) of a non-human antibody. The variable region other than the hypervariable region, e.g., the framework variable region, and the constant region of a humanized antibody are those of a human antibody.

Suitable variable and hypervariable regions of non-human antibodies may be derived from antibodies produced by any non-human mammal in which monoclonal antibodies are made. Suitable examples of mammals other than humans include, for example, rabbits, rats, mice, horses, goats, or primates.

5 Functional equivalents further include fragments of antibodies that have binding characteristics that are the same as, or are comparable to, those of the whole antibody. Suitable fragments of the antibody include any fragment that comprises a sufficient portion of the hypervariable (i.e., complementarity determining) region to bind specifically, and with sufficient affinity, to EGFR tyrosine kinase to inhibit
10 growth of cells that express such receptors.

Such fragments may, for example, contain one or both Fab fragments or the F(ab')₂ fragment. Preferably, the antibody fragments contain all six complementarity determining regions of the whole antibody, although functional fragments containing fewer than all of such regions, such as three, four, or five CDRs, are also included.

15 In one aspect, the fragments are single chain antibodies, or Fv fragments. Single chain antibodies are polypeptides that comprise at least the variable region of the heavy chain of the antibody linked to the variable region of the light chain, with or without an interconnecting linker. Thus, Fv fragment comprises the entire antibody combining site. These chains may be produced in bacteria or in eukaryotic cells.

20 The antibodies and functional equivalents may be members of any class of immunoglobulins, such as IgG, IgM, IgA, IgD, or IgE, and the subclasses thereof. In one aspect, the antibodies are members of the IgG1 subclass. The functional equivalents may also be equivalents of combinations of any of the above classes and subclasses.

25 In one aspect, EGFR antibodies can be selected from chimerized, humanized, fully human, and single chain antibodies derived from the murine antibody 225 described in U.S. Patent No. 4,943,533 to Mendelsohn et al. In one aspect, the 225 derived antibodies have the following hypervariable (CDR) regions of the light and heavy chain, wherein the amino acid sequences are indicated below the nucleotide
30 sequences:

HEAVY CHAIN HYPERVARIABLE REGIONS (VH):

CDR1

AACTATGGTGTACAC (SEQ ID NO: 179)

N Y G V H (SEQ ID NO: 180)

CDR2

5 GTGATATGGAGTGGTGGAAACACAGACTATAATACACCTTTCACATCC
(SEQ ID NO: 181)

V I W S G G N T D Y N T P F T S (SEQ ID NO: 182).

CDR3

GCCCTCACCTACTATGATTACGAGTTTGCTTAC (SEQ ID NO: 183)

10 A L T Y Y D Y E F A Y (SEQ ID NO: 184)

LIGHT CHAIN HYPERVARIABLE REGIONS (VL):

CDR1

AGGGCCAGTCAGAGTATTGGCACAAACATACAC (SEQ ID NO: 185)

15 R A S Q S I G T N I H (SEQ ID NO: 186)

CDR2

GCTTCTGAGTCTATCTCT (SEQ ID NO: 187)

A S E S I S (SEQ ID NO: 188)

CDR3

20 CAACAAAATAATAACTGGCCAACCACG (SEQ ID NO: 189)

Q Q N N N W P T T (SEQ ID NO: 190)

In another aspect, the EGFR antibody can be selected from the antibodies described in U.S. Patent No. 6,235,883 to Jakobovits et al., U.S. Patent No. 5,558,864 to Bendi et al., and U.S. Patent No. 5,891,996 to Mateo de Acosta del Rio et al.

25

In addition to the biological molecules discussed above, the EGFR modulators useful in the invention may also be small molecules. Any molecule that is not a biological molecule is considered herein to be a small molecule. Some examples of small molecules include organic compounds, organometallic compounds, salts of organic and organometallic compounds, saccharides, amino acids, and nucleotides.

30

Small molecules further include molecules that would otherwise be considered biological molecules, except their molecular weight is not greater than 450. Thus,

small molecules may be lipids, oligosaccharides, oligopeptides, and oligonucleotides and their derivatives, having a molecular weight of 450 or less.

It is emphasized that small molecules can have any molecular weight. They are merely called small molecules because they typically have molecular weights less
5 than 450. Small molecules include compounds that are found in nature as well as synthetic compounds. In one embodiment, the EGFR modulator is a small molecule that inhibits the growth of tumor cells that express EGFR. In another embodiment, the EGFR modulator is a small molecule that inhibits the growth of refractory tumor cells that express EGFR.

10 Numerous small molecules have been described as being useful to inhibit EGFR. For example, U.S. Patent No. 5,656,655 to Spada et al. discloses styryl substituted heteroaryl compounds that inhibit EGFR. The heteroaryl group is a monocyclic ring with one or two heteroatoms, or a bicyclic ring with 1 to about 4 heteroatoms, the compound being optionally substituted or polysubstituted.

15 U.S. Patent No. 5,646,153 to Spada et al. discloses bis mono and/or bicyclic aryl heteroaryl, carbocyclic, and heterocarbocyclic compounds that inhibit EGFR.

U.S. Patent No. 5,679,683 to Bridges et al. discloses tricyclic pyrimidine compounds that inhibit the EGFR. The compounds are fused heterocyclic pyrimidine derivatives described at column 3, line 35 to column 5, line 6.

20 U.S. Patent No. 5,616,582 to Barker discloses quinazoline derivatives that have receptor tyrosine kinase inhibitory activity.

Fry et al., Science 265, 1093-1095 (1994) in Figure 1 discloses a compound having a structure that inhibits EGFR.

25 Osharov et al. disclose tyrphostins that inhibit EGFR/HER1 and HER 2, particularly those in Tables I, II, III, and IV.

U.S. Patent No. 5,196,446 to Levitzki et al. discloses heteroarylethenediyl or heteroarylethendeiylaryl compounds that inhibit EGFR, particularly from column 2, line 42 to column 3, line 40.

30 Panek et al., Journal of Pharmacology and Experimental Therapeutics 283, 1433-1444 (1997) discloses a compound identified as PD166285 that inhibits the EGFR, PDGFR, and FGFR families of receptors. PD166285 is identified as 6-(2,6-

dichlorophenyl)-2-(4-(2-diethylaminoethoxy)phenylamino)-8-methyl-8H-pyrido(2,3-d)pyrimidin-7-one having the structure shown in Figure 1 on page 1436.

BIOMARKERS AND BIOMARKER SETS

5 The invention includes individual biomarkers and biomarker sets having both diagnostic and prognostic value in disease areas in which signaling through EGFR or the EGFR pathway is of importance, e.g., in cancers or tumors, in immunological disorders, conditions or dysfunction, or in disease states in which cell signaling and/or cellular proliferation controls are abnormal or aberrant. The biomarker sets comprise
10 a plurality of biomarkers such as, for example, a plurality of the biomarkers provided in Table 4 below, that highly correlate with resistance or sensitivity to one or more EGFR modulators.

 The biomarker sets of the invention enable one to predict or reasonably foretell the likely effect of one or more EGFR modulators in different biological
15 systems or for cellular responses. The biomarker sets can be used in *in vitro* assays of EGFR modulator response by test cells to predict *in vivo* outcome. In accordance with the invention, the various biomarker sets described herein, or the combination of these biomarker sets with other biomarkers or markers, can be used, for example, to predict how patients with cancer might respond to therapeutic intervention with one or
20 more EGFR modulators.

 A biomarker set of cellular gene expression patterns correlating with sensitivity or resistance of cells following exposure of the cells to one or more EGFR modulators provides a useful tool for screening one or tumor samples before treatment with the EGFR modulator. The screening allows a prediction of cells of a tumor
25 sample exposed to one or more EGFR modulators, based on the expression results of the biomarker set, as to whether or not the tumor, and hence a patient harboring the tumor, will or will not respond to treatment with the EGFR modulator.

 The biomarker or biomarker set can also be used as described herein for monitoring the progress of disease treatment or therapy in those patients undergoing
30 treatment for a disease involving an EGFR modulator.

 The biomarkers serve as targets for the development of therapies for disease treatment. Such targets may be particularly applicable to treatment of breast disease,

such as breast cancers or tumors. Indeed, because these biomarkers are differentially expressed in sensitive and resistant cells, their expression patterns are correlated with relative intrinsic sensitivity of cells to treatment with EGFR modulators.

Accordingly, the biomarkers highly expressed in resistant cells may serve as targets
5 for the development of new therapies for the tumors which are resistant to EGFR modulators, particularly EGFR inhibitors.

MICROARRAYS

The invention also includes specialized microarrays, e.g., oligonucleotide
10 microarrays or cDNA microarrays, comprising one or more biomarkers, showing expression profiles that correlate with either sensitivity or resistance to one or more EGFR modulators. Such microarrays can be employed in *in vitro* assays for assessing the expression level of the biomarkers in the test cells from tumor biopsies, and determining whether these test cells are likely to be resistant or sensitive to EGFR
15 modulators. For example, a specialized microarray can be prepared using all the biomarkers, or subsets thereof, as described herein and shown in Table 4. Cells from a tissue or organ biopsy can be isolated and exposed to one or more of the EGFR modulators. Following application of nucleic acids isolated from both untreated and treated cells to one or more of the specialized microarrays, the pattern of gene
20 expression of the tested cells can be determined and compared with that of the biomarker pattern from the control panel of cells used to create the biomarker set on the microarray. Based upon the gene expression pattern results from the cells that underwent testing, it can be determined if the cells show a resistant or a sensitive profile of gene expression. Whether or not the tested cells from a tissue or organ
25 biopsy will respond to one or more of the EGFR modulators and the course of treatment or therapy can then be determined or evaluated based on the information gleaned from the results of the specialized microarray analysis.

ANTIBODIES

30 The invention also includes antibodies, including polyclonal or monoclonal, directed against one or more of the polypeptide biomarkers. Such antibodies can be used in a variety of ways, for example, to purify, detect, and target the biomarkers of

the invention, including both *in vitro* and *in vivo* diagnostic, detection, screening, and/or therapeutic methods.

KITS

5 The invention also includes kits for determining or predicting whether a patient would be susceptible or resistant to a treatment that comprises one or more EGFR modulators. The patient may have a cancer or tumor such as, for example, a breast cancer or tumor. Such kits would be useful in a clinical setting for use in testing a patient's biopsied tumor or cancer samples, for example, to determine or
10 predict if the patient's tumor or cancer will be resistant or sensitive to a given treatment or therapy with an EGFR modulator. The kit comprises a suitable container that comprises: one or more microarrays, e.g., oligonucleotide microarrays or cDNA microarrays, that comprise those biomarkers that correlate with resistance and sensitivity to EGFR modulators, particularly EGFR inhibitors; one or more EGFR
15 modulators for use in testing cells from patient tissue specimens or patient samples; and instructions for use. In addition, kits contemplated by the invention can further include, for example, reagents or materials for monitoring the expression of biomarkers of the invention at the level of mRNA or protein, using other techniques and systems practiced in the art such as, for example, RT-PCR assays, which employ
20 primers designed on the basis of one or more of the biomarkers described herein, immunoassays, such as enzyme linked immunosorbent assays (ELISAs), immunoblotting, e.g., Western blots, or *in situ* hybridization, and the like, as further described herein.

25 APPLICATION OF BIOMARKERS AND BIOMARKER SETS

 The biomarkers and biomarker sets may be used in different applications. Biomarker sets can be built from any combination of biomarkers listed in Table 4 to make predictions about the likely effect of any EGFR modulator in different biological systems. The various biomarkers and biomarker sets described herein can
30 be used, for example, as diagnostic or prognostic indicators in disease management, to predict how patients with cancer might respond to therapeutic intervention with compounds that modulate the EGFR, and to predict how patients might respond to

therapeutic intervention that modulates signaling through the entire EGFR regulatory pathway.

While the data described herein were generated in cell lines that are routinely used to screen and identify compounds that have potential utility for cancer therapy, the biomarkers have both diagnostic and prognostic value in other diseases areas in which signaling through EGFR or the EGFR pathway is of importance, e.g., in immunology, or in cancers or tumors in which cell signaling and/or proliferation controls have gone awry.

In the examples described below, the sensitivity and resistance classifications in the twenty two colon cell lines were similar for the two EGFR modulators tested. Therefore, the biomarkers of the invention are expected to have both diagnostic and prognostic value for other compounds that modulate EGFR or the EGFR signaling pathways.

Those having skill in the pertinent art will appreciate that the EGFR signaling pathway is used and functional in cell types other than cell lines of colon tissue. Therefore, the described biomarkers are expected to have utility for predicting drug sensitivity or resistance to compounds that interact with or inhibit the EGFR activity in cells from other tissues or organs associated with a disease state, or cancers or tumors derived from other tissue types. Non-limiting examples of such cells, tissues and organs include breast, colon, lung, prostate, testes, ovaries, cervix, esophagus, pancreas, spleen, liver, kidney, stomach, lymphocytic and brain, thereby providing a broad and advantageous applicability to the biomarkers described herein. Cells for analysis can be obtained by conventional procedures as known in the art, for example, tissue biopsy, aspiration, sloughed cells, e.g., colonocytes, clinical or medical tissue or cell sampling procedures.

In accordance with the invention, cells from a patient tissue sample, e.g., a tumor or cancer biopsy, can be assayed to determine the expression pattern of one or more biomarkers prior to treatment with one or more EGFR modulators. Success or failure of a treatment can be determined based on the biomarker expression pattern of the cells from the test tissue (test cells), e.g., tumor or cancer biopsy, as being relatively similar or different from the expression pattern of a control set of the one or more biomarkers. Thus, if the test cells show a biomarker expression profile which

corresponds to that of the biomarkers in the control panel of cells which are sensitive to the EGFR modulator, it is highly likely or predicted that the individual's cancer or tumor will respond favorably to treatment with the EGFR modulator. By contrast, if the test cells show a biomarker expression pattern corresponding to that of the biomarkers of the control panel of cells which are resistant to the EGFR modulator, it is highly likely or predicted that the individual's cancer or tumor will not respond to treatment with the EGFR modulator.

The invention also provides a method of monitoring the treatment of a patient having a disease treatable by one or more EGFR modulators. The isolated test cells from the patient's tissue sample, e.g., a tumor biopsy or tumor sample, can be assayed to determine the expression pattern of one or more biomarkers before and after exposure to an EGFR modulator wherein, preferably, the EGFR modulator is an EGFR inhibitor. The resulting biomarker expression profile of the test cells before and after treatment is compared with that of one or more biomarkers as described and shown herein to be highly expressed in the control panel of cells that are either resistant or sensitive to an EGFR modulator. Thus, if a patient's response is sensitive to treatment by an EGFR modulator, based on correlation of the expression profile of the one or biomarkers, the patient's treatment prognosis can be qualified as favorable and treatment can continue. Also, if, after treatment with an EGFR modulator, the test cells don't show a change in the biomarker expression profile corresponding to the control panel of cells that are sensitive to the EGFR modulator, it can serve as an indicator that the current treatment should be modified, changed, or even discontinued. This monitoring process can indicate success or failure of a patient's treatment with an EGFR modulator and such monitoring processes can be repeated as necessary or desired.

The biomarkers of the invention can be used to predict an outcome prior to having any knowledge about a biological system. Essentially, a biomarker can be considered to be a statistical tool. Biomarkers are useful primarily in predicting the phenotype that is used to classify the biological system. In an embodiment of the invention, the goal of the prediction is to classify cancer cells as having an active or inactive EGFR pathway. Cancer cells with an inactive EGFR pathway can be considered resistant to treatment with an EGFR modulator. An inactive EGFR

pathway is defined herein as a non-significant expression of the EGFR or by a classification as "resistant" or "sensitive" based on the IC₅₀ value of each colon cell line to a compound (EGFR inhibitor compound BMS-461453) exemplified herein.

A number of the biomarker described herein are known to be regulated by
5 EGFR, e.g., mucin 2 (J Biol Chem. 2002 Aug 30;277(35):32258-67). Another biomarker, betacellulin, is known to be an EGFR ligand (Biochem Biophys Res Commun. 2002 Jun 28;294(5):1040-6). A functional relationship of the top biomarkers to the EGFR is expected, since biomarkers that contribute to high biomarker accuracy are likely to play a functional role in the pathway that is being
10 modulated. For example, Perception therapy (i.e., antibody that binds to the Her2 receptor and prevents function via internalization) is indicated when the Her2 gene is overexpressed. It is unlikely that a therapy will have any therapeutic effect if the target enzyme is not expressed.

However, although the complete function of all of the biomarkers are not
15 currently known, some of the biomarkers are likely to be directly or indirectly involved in the EGFR signaling pathway. In addition, some of the biomarkers may function in the metabolic or other resistance pathways specific to the EGFR modulators tested. Notwithstanding, knowledge about the function of the biomarkers is not a requisite for determining the accuracy of a biomarker according to the practice
20 of the invention.

DISCOVERY OF BIOMARKERS

An approach has been discovered in which biomarkers were identified whose expression patterns, in a subset of cell lines, correlated to and can be used as an *in*
25 *vitro* marker of cellular response to treatment or therapy with one compound, or with a combination or series of compounds, that are known to inhibit or activate the function of a protein, enzyme, or molecule (e.g., a receptor) that is directly or indirectly involved in cell proliferation, cell responses to external stimuli, (such as ligand binding), or signal transduction, e.g., a receptor tyrosine kinase. Preferred are
30 antagonists or inhibitors of the function of a given protein, e.g., a receptor tyrosine kinase.

Two analytical strategies were deployed to discover biomarkers useful for predicting the sensitivity or resistance of cancer cells to treatment with one or more EGFR modulators. FIG. 1 illustrates the EGFR biomarker identification and prioritization strategy. In one strategy, the mRNA expression level of EGFR was
5 used to identify six colon cancer cell lines with, inferred from the mRNA expression level, no significant presence of the EGFR protein and hence no significant activity of the EGFR pathway (FIG. 2A). In subsequent analyses, biomarkers were identified that had no significant mRNA expression level in the six cell lines and no inferred presence of the EGFR protein. Further, it was required that these biomarkers would
10 have a significant mRNA expression level in at least six other cell lines.

In a second strategy, an EGFR specific tyrosine kinase inhibitor compound was used to determine compound sensitivity in a panel of twenty two colon cancer cell lines following exposure of the cells to the compound. Some of the cell lines were determined to be resistant to treatment with the inhibitor compound, while
15 others were determined to be sensitive to the inhibitor (FIG. 2B). A subset of the cell lines examined provided an expression pattern or profile of biomarkers that correlated to a response by the cells to the EGFR inhibitor compound as well as the absence of significant EGFR expression as thus could serve as biomarkers.

By combining the use of EGFR co-regulation studies in tumor cells with
20 experimental studies in cultured cells as a model of *in vivo* effects, the invention advantageously focuses on cell-intrinsic properties that are exposed in cell culture to identify biomarkers that predict compound sensitivity and resistance. The discovery and identification of biomarkers in tumor cells and cell lines assayed *in vitro* can be used to predict responses to one or more EGFR modulators *in vivo* and, thus, can be
25 extended to clinical situations in which the same biomarkers are used to predict patients' responses to one or more EGFR modulators and treatments comprising one or more EGFR modulators.

As described in the examples below, oligonucleotide microarrays were used to measure the expression levels of over 44,792 probe sets in a panel of thirty one
30 untreated colon cancer cell lines for which the expression status of the EGFR and the drug sensitivity to EGFR inhibitor compounds was determined. This analysis was performed to determine whether the gene expression signatures of untreated cells

were sufficient for the prediction of sensitivity of the disease to inhibition of the EGFR by small molecule or biological molecule compounds. Through data analysis, biomarkers were identified whose expression levels were found to be highly counter-correlated with the status of the EGFR and correlated with the drug sensitivity. In addition, the treatment of cells with a small molecule EGFR inhibitor also provided gene expression signatures predictive of sensitivity to the compound.

The means of performing the gene expression and biomarker identification analyses embraced by the invention is described in further detail and without limitation below.

10

IC₅₀ Determination and Phenotype Classification Based on Sensitivity of Twenty-two Colon Cancer Cell lines to EGFR Inhibitor Compounds

Twenty two colon cell lines were treated with a small molecule EGFR inhibitor (BMS-461453) to determine the individual IC₅₀ value. The IC₅₀ for each cell line was assessed by MTS assays. The average IC₅₀ values along with standard deviations were calculated from two to five individual determinations for each cell line. As shown in FIG. 2B, a 4-fold variation in the IC₅₀ values was observed for the small molecule EGFR inhibitor among the 22 colon cancer cell lines. The IC₅₀ unit is μ M.

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All cell lines with at least a 1.75 fold lower IC₅₀ than the most resistant cell lines were considered to be sensitive to treatment with the small molecule EGFR inhibitor. FIG. 2B represents the resistance/sensitivity classifications of the twenty-two colon cell lines to the small molecule EGFR inhibitor. Five cell lines were classified as sensitive and seventeen cell lines as resistant.

25

Description of the Strategy for Identifying Biomarkers

Biomarkers were discovered based on two criteria: (i) the correlation of their mRNA expression level to the expression of EGFR in cell lines with insignificant EGFR expression and (ii) the correlation of the IC₅₀ values for the small molecule EGFR inhibitor BMS-461453 with gene expression levels.

30

For each of these two biomarker selection strategies, two independent "discovery" probe set lists were established by using statistical filters with different

- stringency levels to identify genes whose expression correlated with either EGFR status or IC₅₀ value. These statistical methods are described below and resulted in four discovery probe set lists: EGFR-A and EGFR-B (correlation with no significant EGFR expression) and IC-50-A, IC-50-B (correlation with IC₅₀ expression), the A-
- 5 lists containing probe sets selected by more stringent conditions. To then establish two biomarker probe set lists, probe sets that appeared in both EGFR-A and IC-50 B were selected (Biomarker Probe Set List A, Table 2) and probe sets that appeared in both EGFR-B and IC-50-A were selected (Biomarker Probe Set List B, Table 3).
- 10 Identifying Genes that Significantly Correlate with EGFR status classification
- RT-PCR expression data for EGFR were obtained from thirty one colon cancer cell lines and six cell lines with a significantly lower expression level of EGFR compared to the other cell lines were identified as described in Example 1 below. (FIG. 2A). Expression profiling data of 44,792 probe sets represented on the HG-
- 15 U133 array set for all thirty one untreated colon cancer cell lines were obtained and analyzed for the identification of probe sets which would be correlated with the above described six cell lines with no significant mRNA expression of EGFR. For the discovery probe set list EGFR-A, all probe sets which were judged to be absent by the Affymetrix Mas 5.0 software in six of the six colon cancer cell lines with significantly
- 20 lower expression of EGFR were identified. Second, it was required that these probe sets would be judged to be present in at least six cell lines of the twenty five cell lines classified as having significant mRNA expression of the EGFR. This analytical strategy resulted in the identification of 280 probe sets that could be analyzed in comparison to the discovery probe set list IC-50-B.
- 25 The discovery probe set list EGFR-B was generated by selecting all probe sets which were judged to be absent by the Affymetrix Mas 5.0 software in five of the six colon cancer cell lines with significantly lower expression of EGFR and which would be present in at least six cell lines of the twenty five cell lines classified as having significant mRNA expression of the EGFR. Discovery probe set list EGR-B contains
- 30 1,852 probe sets (U133A: 876; U133B: 976).

Identifying Genes that Significantly Correlate with Drug Resistance/Sensitivity Classification

Expression profiling data of 44,792 probe sets represented on the HG-U133 array set for twenty two untreated colon cell lines were obtained and preprocessed as described in Example 1 below. These data were analyzed using the Student's TTEST to identify genes whose expression patterns were strongly correlated with the drug resistance/sensitivity classification. Table 1 provides the resistance/sensitivity phenotype classification of the twenty two colon cell lines for the EGFR antagonist BMS-461453 based on the IC_{50} results. The mean IC_{50} values along with standard deviations (SD) were calculated from 2 to 5 individual determinations for each cell line as shown. The mean IC_{50} across the twenty two colon cell lines for BMS-461453 was calculated and used to normalize the IC_{50} data for each cell line. All cell lines with at least a 1.75 fold lower IC_{50} than the most resistant cell lines were considered to be sensitive to treatment with BMS-461453. The cell lines designated with an asterisk are defined as being sensitive to the drug treatment.

TABLE 1 - Resistance/Sensitivity Phenotype Classification of Twenty Two Colon Cell Lines

Cell lines	IC ₅₀ (μM)	SD
CCD_33C0*	2	1.28
LOVO*	2.3	2.28
LS174T*	3.5	1.93
Caco2*	5.5	3.97
SW403*	5.7	4.94
CCD18Co	7.1	3.84
SW837	7.2	3.30
Sk-Co-1	9	2.02
MIP	9.7	0.52
SW1417	10	0.00
HT-29	10	0.00
T84	10	0.00
CX-1	10	0.00
Colo-205	10	0.00
Colo-201	10	0.00
Colo320HSR	10	0.00
HCT8	10	0.00
Colo320DM	10	0.00
SW480	10	0.00
HCT116	10	0.00
SW620	10	0.00
HCT116S542	10	0.00

An "idealized expression pattern" corresponds to a gene that is uniformly high in one class (e.g., sensitive) and uniformly low in the other (e.g., resistant). Initially, a Student TTEST was performed in which a T value was obtained for each probe set.

- 5 Once a T value was generated, its corresponding confidence value (P) was found on a standard table of significance. The confidence value is a measure of the probability to observe a certain mean expression difference between two groups by chance alone and is obtained using the following formula:

$$T(g,c) = (X_1 - X_2) / (\text{var}_1/n_1 + \text{var}_2/n_2)^{1/2}$$

wherein,

$T(g,c)$ represents the T value between expression for gene g and the sensitivity/resistance classification c;

5 X_1 represents mean gene expression level of samples in class 1;

X_2 represents mean gene expression level of samples in class 2;

var_1 represents variance of gene expression for samples in class 1;

var_2 represents variance of gene expression for samples in class 2;

n_1 represents number of samples in class 1;

10 n_2 represents number of samples in class 2; and

corresponding confidence value (P) for T values are obtained from a standard table of significance.

To generate discovery probe set list IC-50-B, a confidence value of 0.05 or lower was used as the cut off for probe sets to be included in the list. Discovery probe
15 set list IC-50-B contains 5,050 probe sets (U133A: 2,498; U133B: 2,552).

Discovery probe set list IC-50-A was generated using the Pearson correlation coefficient (a dimensionless index that ranges from -1.0 to 1.0). This value was calculated by treating the IC₅₀ data as continuous variables and by utilizing a linear regression model to correlate gene expression levels with IC₅₀ values for twenty-two
20 colon cell lines. Probe sets with a correlation coefficient less than -0.5 were selected (p < 0.02), a total of 902 probe sets (U133A: 467; U133B: 435).

Finally, two separate biomarker probe set lists were generated, biomarker probe set lists A and B, by identifying probe sets which were present in EGFR-A and IC-50-B (Biomarker Probe Set List A) (Table 2) or were present in EGFR-B and IC-
25 50-A (Biomarker Probe Set List B) (Table 3).

The biomarker probe set list A (Table 2) contains a total of 74 probe sets (U133A: 43; U133B: 31) and provides the polynucleotides identified to be biomarkers of EGFR antagonist sensitivity employing strategy A. With strategy A, polynucleotides were required to satisfy a stringent criteria for EGFR status
30 coregulation and a less stringent condition for correlation to IC₅₀ values. Namely, the polynucleotides had to be called absent by the Affymetrix software in six out of the

six cell lines with lowest expression of EGFR and be differentially expressed in the sensitive and resistance cell lines with a P value equal to or less than 0.05.

TABLE 2 - Biomarker Probe Set List A

Unigene Title	Affymetrix Description	Affymetrix probe set
hemoglobin, alpha 1	gb:BC005931.1 /DEF=Homo sapiens, hemoglobin, alpha 2, clone MGC:14541, mRNA, complete cds. /FEA=mRNA /PROD=hemoglobin, alpha 2 /DB_XREF=gi:13543547 /FL=gb:BC005931.1	211745_x_at
dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2)	gb:M80536.1 /DEF=H.sapiens dipeptidyl peptidase IV (DPP4) mRNA, complete cds. /FEA=mRNA /GEN=DPP4 /PROD=dipeptidyl peptidase IV /DB_XREF=gi:181569 /UG=Hs.44926 dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) /FL=gb:M80536.1 gb:Nm_001935.1	203716_s_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213994_s_at
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)	gb:Nm_005518.1 /DEF=Homo sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) (HMGCS2), mRNA. /FEA=mRNA /GEN=HMGCS2 /PROD=3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2(mitochondrial) /DB_XREF=gi:5031750 /UG=Hs.59889 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /FL=gb:Nm_005518.1	204607_at
mucin 2, intestinal/trachea 1	gb:Nm_002457.1 /DEF=Homo sapiens mucin 2, intestinaltracheal (MUC2), mRNA. /FEA=mRNA /GEN=MUC2 /PROD=mucin 2, intestinaltracheal /DB_XREF=gi:4505284 /UG=Hs.315 mucin 2, intestinaltracheal /FL=gb:Nm_002457.1 gb:L21998.1	204673_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	gb:Nm_000492.2 /DEF=Homo sapiens cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) (CFTR), mRNA. /FEA=mRNA /GEN=CFTR /PROD=cystic fibrosis transmembrane conductanceregulator, ATP-binding cassette (sub-family C, member 7) /DB_XREF=gi:6995995	205043_at

	/UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /FL=gb:NM_000492.2	
CUG triplet repeat, RNA-binding protein 2	Consensus includes gb:N36839 /FEA=EST /DB_XREF=gi:1157981 /DB_XREF=est:yy35f07.s1 /CLONE=IMAGE:273253 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202156_s_at
nuclear receptor subfamily 3, group C, member 2	gb:NM_000901.1 /DEF=Homo sapiens nuclear receptor subfamily 3, group C, member 2 (NR3C2), mRNA. /FEA=mRNA /GEN=NR3C2 /PROD=nuclear receptor subfamily 3, group C, member 2 /DB_XREF=gi:4505198 /UG=Hs.1790 nuclear receptor subfamily 3, group C, member 2 /FL=gb:M16801.1 gb:NM_000901.1	205259_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215702_s_at
cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2	gb:NM_000775.1 /DEF=Homo sapiens cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 (CYP2J2), mRNA. /FEA=mRNA /GEN=CYP2J2 /PROD=cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 /DB_XREF=gi:4503226 /UG=Hs.152096 cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 /FL=gb:U37143.1 gb:NM_000775.1	205073_at
cystatin S	gb:NM_001899.1 /DEF=Homo sapiens cystatin S (CST4), mRNA. /FEA=mRNA /GEN=CST4 /PROD=cystatin S /DB_XREF=gi:4503108 /UG=Hs.56319 cystatin S /FL=gb:NM_001899.1	206994_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213993_at
fibroblast growth factor receptor 2 (bacteria-expressed kinase,	gb:NM_022969.1 /DEF=Homo sapiens fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome,	203638_s_at

keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2), transcript variant 2, mRNA. /FEA=mRNA /GEN=FGFR2 /PROD=fibroblast growth factor receptor 2, isoform 2precursor /DB_XREF=gi:13186252 /UG=Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) /FL=gb:NM_022969.1 gb:M97193.1 gb:M80634.1	
mucin 3B	Consensus includes gb:AB038783.1 /DEF=Homo sapiens MUC3B mRNA for intestinal mucin, partial cds. /FEA=mRNA /GEN=MUC3B /PROD=intestinal mucin /DB_XREF=gi:9929917 /UG=Hs.129782 mucin 3A, intestinal	214898_x_at
AA	Consensus includes gb:AV728958 /FEA=EST /DB_XREF=gi:10838379 /DB_XREF=est:AV728958 /CLONE=HTCBYF04 /UG=Hs.150443 KIAA0320 protein	212703_at
CUG triplet repeat, RNA-binding protein 2	gb:NM_006561.1 /DEF=Homo sapiens CUG triplet repeat, RNA-binding protein 2 (CUGBP2), mRNA. /FEA=mRNA /GEN=CUGBP2 /PROD=CUG triplet repeat, RNA-binding protein 2 /DB_XREF=gi:5729815 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202158_s_at
spondin 1, (f-spondin) extracellular matrix protein	gb:AB051390.1 /DEF=Homo sapiens mRNA for VSGPF-spondin, complete cds. /FEA=mRNA /PROD=VSGPF-spondin /DB_XREF=gi:11320819 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein /FL=gb:AB051390.1	209437_s_at
mucin 3B	Consensus includes gb:AF113616 /DEF=Homo sapiens intestinal mucin 3 (MUC3) gene, partial cds /FEA=mRNA /DB_XREF=gi:6466800 /UG=Hs.129782 mucin 3A, intestinal	214676_x_at
EphA1	gb:NM_005232.1 /DEF=Homo sapiens EphA1 (EPHA1), mRNA. /FEA=mRNA /GEN=EPHA1 /PROD=EphA1 /DB_XREF=gi:4885208 /UG=Hs.89839 EphA1 /FL=gb:M18391.1 gb:NM_005232.1	205977_s_at
matrilin 3	gb:NM_002381.2 /DEF=Homo sapiens matrilin 3 (MATN3) precursor, mRNA. /FEA=mRNA /GEN=MATN3 /PROD=matrilin 3 precursor /DB_XREF=gi:13518040 /UG=Hs.278461	206091_at

	matrilin 3 /FL=gb:NM_002381.2	
bone morphogenetic protein 2	gb:NM_001200.1 /DEF=Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA. /FEA=mRNA /GEN=BMP2 /PROD=bone morphogenetic protein 2 precursor /DB_XREF=gi:4557368 /UG=Hs.73853 bone morphogenetic protein 2 /FL=gb:NM_001200.1	205290_s_at
interferon consensus sequence binding protein 1	Consensus includes gb:AI073984 /FEA=EST /DB_XREF=gi:3400628 /DB_XREF=est:oy66c05.x1 /CLONE=IMAGE:1670792 /UG=Hs.14453 interferon consensus sequence binding protein 1 /FL=gb:M91196.1 gb:NM_002163.1	204057_at
retinoic acid receptor responder (tazarotene induced) 1	Consensus includes gb:AI669229 /FEA=EST /DB_XREF=gi:4834003 /DB_XREF=est:wc13e06.x1 /CLONE=IMAGE:2315074 /UG=Hs.82547 retinoic acid receptor responder (tazarotene induced) 1	221872_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215703_at
fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	gb:M87771.1 /DEF=Human secreted fibroblast growth factor receptor (K-sam-III) mRNA, complete cds. /FEA=mRNA /GEN=K-sam-III /PROD=fibroblast growth factor receptor /DB_XREF=gi:186781 /UG=Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) /FL=gb:NM_022970.1 gb:M87771.1	208228_s_at
myosin, heavy polypeptide 13, skeletal muscle	gb:NM_003802.1 /DEF=Homo sapiens myosin, heavy polypeptide 13, skeletal muscle (MYH13), mRNA. /FEA=mRNA /GEN=MYH13 /PROD=myosin, heavy polypeptide 13, skeletal muscle /DB_XREF=gi:11321578 /UG=Hs.278488 myosin, heavy polypeptide 13, skeletal muscle /FL=gb:NM_003802.1	208208_at

	gb:AF111782.2	
ESTs, Weakly similar to I38022 hypothetical protein [H.sapiens]	Consensus includes gb:AW675655 /FEA=EST /DB_XREF=gi:7540890 /DB_XREF=est:ba52e01.x1 /CLONE=IMAGE:2900184 /UG=Hs.314158 ESTs	222354_at
hypothetical protein FLJ20174	gb:Nm_017699.1 /DEF=Homo sapiens hypothetical protein FLJ20174 (FLJ20174), mRNA. /FEA=mRNA /GEN=FLJ20174 /PROD=hypothetical protein FLJ20174 /DB_XREF=gi:8923170 /UG=Hs.114556 hypothetical protein FLJ20174 /FL=gb:Nm_017699.1	219734_at
PTPRF interacting protein, binding protein 2 (liprin beta 2)	Consensus includes gb:AI692180 /FEA=EST /DB_XREF=gi:4969520 /DB_XREF=est:wd37f06.x1 /CLONE=IMAGE:2330339 /UG=Hs.12953 PTPRF interacting protein, binding protein 2 (liprin beta 2)	212841_s_at
ribonuclease, RNase A family, 1 (pancreatic)	gb:Nm_002933.1 /DEF=Homo sapiens ribonuclease, RNase A family, 1 (pancreatic) (RNASE1), mRNA. /FEA=mRNA /GEN=RNASE1 /PROD=ribonuclease, RNase A family, 1 (pancreatic) /DB_XREF=gi:4506546 /UG=Hs.78224 ribonuclease, RNase A family, 1 (pancreatic) /FL=gb:BC005324.1 gb:Nm_002933.1 gb:D26129.1	201785_at
hairless (mouse) homolog	gb:Nm_018411.1 /DEF=Homo sapiens hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) (HSA277165), mRNA. /FEA=mRNA /GEN=HSA277165 /PROD=hairless protein /DB_XREF=gi:11036651 /UG=Hs.272367 hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) /FL=gb:Nm_018411.1	220163_s_at
nuclear receptor subfamily 5, group A, member 2	Consensus includes gb:AF228413.1 /DEF=Homo sapiens hepatocyte transcription factor mRNA, 3'UTR. /FEA=mRNA /DB_XREF=gi:7677372 /UG=Hs.183123 nuclear receptor subfamily 5, group A, member 2 /FL=gb:U93553.1 gb:AB019246.1 gb:AF124247.1	210174_at
superoxide dismutase 3, extracellular	gb:Nm_003102.1 /DEF=Homo sapiens superoxide dismutase 3, extracellular (SOD3), mRNA. /FEA=mRNA /GEN=SOD3 /PROD=superoxide dismutase 3, extracellular	205236_x_at

	/DB_XREF=gi:4507150 /UG=Hs.2420 superoxide dismutase 3, extracellular /FL=gb:J02947.1 gb:Nm_003102.1	
zinc finger protein 137 (clone pHZ-30)	gb:Nm_003438.1 /DEF=Homo sapiens zinc finger protein 137 (clone pHZ-30) (ZNF137), mRNA. /FEA=mRNA /GEN=ZNF137 /PROD=zinc finger protein 137 (clone pHZ-30) /DB_XREF=gi:4507988 /UG=Hs.151689 zinc finger protein 137 (clone pHZ-30) /FL=gb:Nm_003438.1 gb:U09414.1	207394_at
Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042)	Consensus includes gb:AL049983.1 /DEF=Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042). /FEA=mRNA /DB_XREF=gi:4884234 /UG=Hs.240136 Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042)	217288_at
Hermansky- Pudlak syndrome	Consensus includes gb:AL022313 /DEF=Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3 Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3- P66), the gene f... /FEA=CDS_3 /DB_XREF=gi:4200326 /UG=Hs.272270 Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3 Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3- P66), the gene for a nov	217354_s_at
peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase	gb:Nm_018441.1 /DEF=Homo sapiens peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase (HSA250303), mRNA. /FEA=mRNA /GEN=HSA250303 /PROD=peroxisomal trans 2- enoyl CoA reductase; putative short chain alcohol dehydrogenase /DB_XREF=gi:8923751 /UG=Hs.281680 peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase /FL=gb:Nm_018441.1	221142_s_at
BTG family, member 2	gb:Nm_006763.1 /DEF=Homo sapiens BTG family, member 2 (BTG2), mRNA. /FEA=mRNA /GEN=BTG2 /PROD=BTG family, member 2 /DB_XREF=gi:5802987 /UG=Hs.75462 BTG family, member 2 /FL=gb:U72649.1 gb:Nm_006763.1	201236_s_at
phosducin	gb:M33478.1 /DEF=Human 33-kDa phototransducing protein mRNA, complete cds.	211496_s_at

	/FEA=mRNA /DB_XREF=gi:177186 /UG=Hs.550 phosducin /FL=gb:NM_022577.1 gb:M33478.1 gb:AF076465.1	
Rho GTPase activating protein 8	gb:NM_015366.1 /DEF=Homo sapiens Rho GTPase activating protein 8 (ARHGAP8), mRNA. /FEA=mRNA /GEN=ARHGAP8 /PROD=Rho GTPase activating protein 8 /DB_XREF=gi:7656903 /UG=Hs.102336 Rho GTPase activating protein 8 /FL=gb:NM_015366.1	205980_s_at
Homo sapiens clone 24707 mRNA sequence	Consensus includes gb:AW593996 /FEA=EST /DB_XREF=gi:7281254 /DB_XREF=est:hg41g06.x1 /CLONE=IMAGE:2948218 /UG=Hs.124969 Homo sapiens clone 24707 mRNA sequence	213256_at
caspase 10, apoptosis-related cysteine protease	gb:NM_001230.1 /DEF=Homo sapiens caspase 10, apoptosis-related cysteine protease (CASP10), mRNA. /FEA=mRNA /GEN=CASP10 /PROD=caspase 10, apoptosis- related cysteine protease /DB_XREF=gi:4502568 /UG=Hs.5353 caspase 10, apoptosis-related cysteine protease /FL=gb:U60519.1 gb:NM_001230.1	205467_at
KIAA0690 protein	Consensus includes gb:AK000238.1 /DEF=Homo sapiens cDNA FLJ20231 fis, clone COLF5511, highly similar to AB014590 Homo sapiens mRNA for KIAA0690 protein. /FEA=mRNA /DB_XREF=gi:7020188 /UG=Hs.60103 KIAA0690 protein	216360_x_at
Homo sapiens, Similar to RIKEN cDNA 1810037C20 gene, clone MGC:21481 IMAGE:385206 2, mRNA, complete cds	Consensus includes gb:AW001287 /FEA=EST /DB_XREF=gi:5848203 /DB_XREF=est:wu27e06.x1 /CLONE=IMAGE:2521282 /UG=Hs.61265 ESTs, Weakly similar to G786_HUMAN PROTEIN GS3786 H.sapiens	227676_at
ESTs	Consensus includes gb:AA581439 /FEA=EST /DB_XREF=gi:2359211 /DB_XREF=est:nh13c10.s1 /CLONE=IMAGE:952242 /UG=Hs.152328 ESTs	244650_at
ESTs	Consensus includes gb:AI739241 /FEA=EST /DB_XREF=gi:5101222 /DB_XREF=est:wi14h02.x1 /CLONE=IMAGE:2390259 /UG=Hs.171480 ESTs	238984_at

hypothetical protein FLJ23045	Consensus includes gb:AB046810.1 /DEF=Homo sapiens mRNA for KIAA1590 protein, partial cds. /FEA=mRNA /GEN=KIAA1590 /PROD=KIAA1590 protein /DB_XREF=gi:10047254 /UG=Hs.101774 hypothetical protein FLJ23045	232083_at
regenerating gene type IV	gb:AY007243.1 /DEF=Homo sapiens regenerating gene type IV mRNA, complete cds. /FEA=mRNA /PROD=regenerating gene type IV /DB_XREF=gi:12621025 /UG=Hs.105484 Homo sapiens regenerating gene type IV mRNA, complete cds /FL=gb:AY007243.1	223447_at
ESTs	Consensus includes gb:AI139990 /FEA=EST /DB_XREF=gi:3647447 /DB_XREF=est:qa47d03.x1 /CLONE=IMAGE:1689893 /UG=Hs.134586 ESTs	231022_at
ESTs	Consensus includes gb:AI733801 /FEA=EST /DB_XREF=gi:5054914 /DB_XREF=est:qk39c04.x5 /CLONE=IMAGE:1871334 /UG=Hs.146186 ESTs	237923_at
hypothetical protein MGC20702	Consensus includes gb:AK002203.1 /DEF=Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786. /FEA=mRNA /DB_XREF=gi:7023932 /UG=Hs.10260 Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786	226992_at
ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINAT ION WARNING ENTRY [H.sapiens]	Consensus includes gb:AI457984 /FEA=EST /DB_XREF=gi:4312002 /DB_XREF=est:tj66a04.x1 /CLONE=IMAGE:2146446 /UG=Hs.165900 ESTs, Weakly similar to ALUC_HUMAN !!!! ALU CLASS C WARNING ENTRY !!! H.sapiens	243729_at
Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	Consensus includes gb:T86159 /FEA=EST /DB_XREF=gi:714511 /DB_XREF=est:yd84h07.s1 /CLONE=IMAGE:114973 /UG=Hs.10450 Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	227724_at
ESTs	Consensus includes gb:AI806131 /FEA=EST /DB_XREF=gi:5392697 /DB_XREF=est:wf06c06.x1 /CLONE=IMAGE:2349802 /UG=Hs.99376	231148_at

	ESTs	
anterior gradient 2 (Xenopus laevis) homolog	Consensus includes gb:AI922323 /FEA=EST /DB_XREF=gi:5658287 /DB_XREF=est:wn90h03.x1 /CLONE=IMAGE:2453141 /UG=Hs.293380 ESTs	228969_at
ESTs	Consensus includes gb:AI493909 /FEA=EST /DB_XREF=gi:4394912 /DB_XREF=est:qz94e02.x1 /CLONE=IMAGE:2042234 /UG=Hs.6131 ESTs	235562_at
hypothetical protein FLJ22233	Consensus includes gb:AI339568 /FEA=EST /DB_XREF=gi:4076495 /DB_XREF=est:qk67e10.x1 /CLONE=IMAGE:1874058 /UG=Hs.286194 hypothetical protein FLJ22233 /FL=gb:NM_024959.1	222727_s_at
GalNAc alpha-2, 6-sialyltransferase I, long form	Consensus includes gb:Y11339.2 /DEF=Homo sapiens mRNA for GalNAc alpha-2, 6-sialyltransferase I, long form. /FEA=mRNA /PROD=GalNAc alpha-2,6-sialyltransferase I /DB_XREF=gi:7576275 /UG=Hs.105352 GalNAc alpha-2, 6-sialyltransferase I, long form	227725_at
ESTs	Consensus includes gb:AI917390 /FEA=EST /DB_XREF=gi:5637245 /DB_XREF=est:ts79a05.x1 /CLONE=IMAGE:2237456 /UG=Hs.99415 ESTs	240964_at
Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA	Consensus includes gb:AK026404.1 /DEF=Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA. /FEA=mRNA /DB_XREF=gi:10439257 /UG=Hs.271819 Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA	232321_at
Homo sapiens cDNA: FLJ23331 fis, clone HEP12664	Consensus includes gb:AK026984.1 /DEF=Homo sapiens cDNA: FLJ23331 fis, clone HEP12664. /FEA=mRNA /DB_XREF=gi:10439980 /UG=Hs.50742 Homo sapiens cDNA: FLJ23331 fis, clone HEP12664	229021_at
ESTs	Consensus includes gb:AA827649 /FEA=EST /DB_XREF=gi:2900090 /DB_XREF=est:od01a12.s1 /CLONE=IMAGE:1357918 /UG=Hs.105317 ESTs	235515_at
prostate cancer	Consensus includes gb:AA633076 /FEA=EST	226167_at

associated protein 7	/DB_XREF=gi:2556490 /DB_XREF=est:nq38a06.s1 /CLONE=IMAGE:1146130 /UG=Hs.27495 prostate cancer associated protein 7	
ESTs	Consensus includes gb:N37023 /FEA=EST /DB_XREF=gi:1158165 /DB_XREF=est:yy40d03.s1 /CLONE=IMAGE:273701 /UG=Hs.235883 ESTs	225407_at
ESTs, Weakly similar to I38588 reverse transcriptase homolog [H.sapiens]	Consensus includes gb:AI864053 /FEA=EST /DB_XREF=gi:5528160 /DB_XREF=est:wj55h10.x1 /CLONE=IMAGE:2406787 /UG=Hs.39972 ESTs, Weakly similar to I38588 reverse transcriptase homolog H.sapiens	235678_at
ESTs, Weakly similar to JX0331 laurate omega-hydroxylase [H.sapiens]	Consensus includes gb:AA557324 /FEA=EST /DB_XREF=gi:2327801 /DB_XREF=est:nl81a02.s1 /CLONE=IMAGE:1057034 /UG=Hs.26040 ESTs, Weakly similar to fatty acid omega-hydroxylase H.sapiens	227702_at
ESTs	Consensus includes gb:BF594323 /FEA=EST /DB_XREF=gi:11686647 /DB_XREF=est:7h79g07.x1 /CLONE=IMAGE:3322236 /UG=Hs.158989 ESTs	238103_at
ESTs, Weakly similar to JE0350 Anterior gradient-2 [H.sapiens]	Consensus includes gb:AI827789 /FEA=EST /DB_XREF=gi:5448449 /DB_XREF=est:wf33a07.x1 /CLONE=IMAGE:2357364 /UG=Hs.100686 ESTs, Weakly similar to JE0350 Anterior gradient-2 H.sapiens	228241_at
ESTs	Consensus includes gb:AI968097 /FEA=EST /DB_XREF=gi:5764915 /DB_XREF=est:wu13a12.x1 /CLONE=IMAGE:2516830 /UG=Hs.131360 ESTs	237835_at
ESTs	Consensus includes gb:H05025 /FEA=EST /DB_XREF=gi:868577 /DB_XREF=est:yl74g12.s1 /CLONE=IMAGE:43864 /UG=Hs.323767 ESTs	241874_at
Homo sapiens, Similar to RIKEN cDNA 1110060O18 gene, clone MGC:17236 IMAGE:386413	Consensus includes gb:AA524690 /FEA=EST /DB_XREF=gi:2265618 /DB_XREF=est:ng38e07.s1 /CLONE=IMAGE:937092 /UG=Hs.294143 ESTs, Weakly similar to predicted using Genefinder C.elegans	226168_at

7, mRNA, complete cds		
ESTs	Consensus includes gb:AI300126 /FEA=EST /DB_XREF=gi:3959472 /DB_XREF=est:qn54f02.x1 /CLONE=IMAGE:1902075 /UG=Hs.257858 ESTs	240830_at
Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	Consensus includes gb:AA129774 /FEA=EST /DB_XREF=gi:1690185 /DB_XREF=est:zl16h09.s1 /CLONE=IMAGE:502145 /UG=Hs.288905 Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	227019_at
ESTs	Consensus includes gb:AW024656 /FEA=EST /DB_XREF=gi:5878186 /DB_XREF=est:wu78h05.x1 /CLONE=IMAGE:2526201 /UG=Hs.233382 ESTs, Moderately similar to AF119917 62 PRO2822 H.sapiens	242358_at

The biomarker probe set list B (Table 3) contains 95 probe sets (U133A: 47; U133B 48). The biomarker probe set list B contains polynucleotides identified to be biomarkers of EGFR antagonist sensitivity employing strategy B. In strategy B, polynucleotides were required to satisfy a stringent criteria for correlation to IC₅₀ values and a less stringent condition for EGFR status coregulation. Namely, the polynucleotides had to have a Pearsons correlation of -0.5 or less with respect to IC₅₀ and be called absent by the Affymetrix software in 5 out of the 6 cell lines with lowest expression of EGFR.

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TABLE 3 - Biomarker Probe Set List B

Unigene Title	Affymetrix Description	Affymetrix probe set
dopa decarboxylase (aromatic L- amino acid decarboxylase)	Consensus includes gb:AW772056 /FEA=EST /DB_XREF=gi:7704118 /DB_XREF=est:hn64g06.x1 /CLONE=IMAGE:3032698 /UG=Hs.150403 dopa decarboxylase (aromatic L-amino acid decarboxylase)	214347_s_at
cystic fibrosis transmembrane conductance regulator, ATP- binding cassette	gb:NM_000492.2 /DEF=Homo sapiens cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) (CFTR), mRNA. /FEA=mRNA /GEN=CFTR /PROD=cystic fibrosis transmembrane	205043_at

(sub-family C, member 7)	conductance regulator, ATP-binding cassette (sub-family C, member 7) /DB_XREF=gi:6995995 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /FL=gb:NM_000492.2	
carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen)	gb:BC005008.1 /DEF=Homo sapiens, carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen), clone MGC:10467, mRNA, complete cds. /FEA=mRNA /PROD=carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) /DB_XREF=gi:13477106 /UG=Hs.73848 carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) /FL=gb:BC005008.1 gb:M18216.1 gb:M29541.1 gb:NM_002483.1	203757_s_at
hypothetical protein FLJ20075	gb:NM_017655.1 /DEF=Homo sapiens hypothetical protein FLJ20075 (FLJ20075), mRNA. /FEA=mRNA /GEN=FLJ20075 /PROD=hypothetical protein FLJ20075 /DB_XREF=gi:8923083 /UG=Hs.205058 hypothetical protein FLJ20075 /FL=gb:NM_017655.1	219970_at
ATPase, Class V, type 10B	Consensus includes gb:AW006935 /FEA=EST /DB_XREF=gi:5855713 /DB_XREF=est:wt08b11.x1 /CLONE=IMAGE:2506845 /UG=Hs.109358 ATPase, Class V, type 10B	214070_s_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215702_s_at
HERV-H LTR-associating 2	gb:NM_007072.1 /DEF=Homo sapiens HERV-H LTR-associating 2 (HHLA2), mRNA. /FEA=mRNA /GEN=HHLA2 /PROD=HERV-H LTR-associating 2 /DB_XREF=gi:5901963 /UG=Hs.252351 HERV-H LTR-associating 2 /FL=gb:AF126162.1 gb:NM_007072.1	220812_s_at
AA	Consensus includes gb:AV728958 /FEA=EST /DB_XREF=gi:10838379 /DB_XREF=est:AV728958 /CLONE=HTCBYF04 /UG=Hs.150443 KIAA0320 protein	212703_at

hemoglobin, alpha 2	Consensus includes gb:T50399 /FEA=EST /DB_XREF=gi:652259 /DB_XREF=est:yb30b11.s1 /CLONE=IMAGE:72669 /UG=Hs.251577 hemoglobin, alpha 1	214414_x_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213993_at
hemoglobin, alpha 1	gb:BC005931.1 /DEF=Homo sapiens, hemoglobin, alpha 2, clone MGC:14541, mRNA, complete cds. /FEA=mRNA /PROD=hemoglobin, alpha 2 /DB_XREF=gi:13543547 /FL=gb:BC005931.1	211745_x_at
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5	gb:Nm_002639.1 /DEF=Homo sapiens serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5), mRNA. /FEA=mRNA /GEN=SERPINB5 /PROD=serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 /DB_XREF=gi:4505788 /UG=Hs.55279 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 /FL=gb:Nm_002639.1 gb:U04313.1	204855_at
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)	gb:Nm_005518.1 /DEF=Homo sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) (HMGCS2), mRNA. /FEA=mRNA /GEN=HMGCS2 /PROD=3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /DB_XREF=gi:5031750 /UG=Hs.59889 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /FL=gb:Nm_005518.1	204607_at
anterior gradient 2 (Xenopus laevis) homolog	gb:AF088867.1 /DEF=Homo sapiens putative secreted protein XAG mRNA, complete cds. /FEA=mRNA /PROD=putative secreted protein XAG /DB_XREF=gi:6652811 /UG=Hs.91011 anterior gradient 2 (Xenopus laevis) homolog /FL=gb:AF007791.1 gb:AF038451.1 gb:Nm_006408.1 gb:AF088867.1	209173_at
FXRD domain-containing ion transport regulator 3	gb:BC005238.1 /DEF=Homo sapiens, FXRD domain-containing ion transport regulator 3, clone MGC:12265, mRNA, complete cds. /FEA=mRNA /PROD=FXRD domain-containing ion transport regulator3 /DB_XREF=gi:13528881 /UG=Hs.301350 FXRD domain-containing ion transport regulator	202489_s_at

	3 /FL=gb:NM_005971.2 gb:BC005238.1	
dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2)	gb:M80536.1 /DEF=H.sapiens dipeptidyl peptidase IV (DPP4) mRNA, complete cds. /FEA=mRNA /GEN=DPP4 /PROD=dipeptidyl peptidase IV /DB_XREF=gi:181569 /UG=Hs.44926 dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) /FL=gb:M80536.1 gb:NM_001935.1	203716_s_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215703_at
EphA1	gb:NM_005232.1 /DEF=Homo sapiens EphA1 (EPHA1), mRNA. /FEA=mRNA /GEN=EPHA1 /PROD=EphA1 /DB_XREF=gi:4885208 /UG=Hs.89839 EphA1 /FL=gb:M18391.1 gb:NM_005232.1	205977_s_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213994_s_at
CUG triplet repeat, RNA-binding protein 2	gb:NM_006561.1 /DEF=Homo sapiens CUG triplet repeat, RNA-binding protein 2 (CUGBP2), mRNA. /FEA=mRNA /GEN=CUGBP2 /PROD=CUG triplet repeat, RNA-binding protein 2 /DB_XREF=gi:5729815 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202158_s_at
DKFZP434C091 protein	Consensus includes gb:AL080170.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C091 (from clone DKFZp434C091); partial cds. /FEA=mRNA /GEN=DKFZp434C091 /PROD=hypothetical protein /DB_XREF=gi:5262639 /UG=Hs.51692 DKFZP434C091 protein	215047_at
mucin 3B	Consensus includes gb:AF113616 /DEF=Homo sapiens intestinal mucin 3 (MUC3) gene, partial cds /FEA=mRNA /DB_XREF=gi:6466800 /UG=Hs.129782 mucin 3A, intestinal	214676_x_at
potassium channel,	gb:U90065.1 /DEF=Human potassium channel KCNO1 mRNA, complete cds. /FEA=mRNA	204678_s_at

subfamily K, member 1 (TWIK-1)	/PROD=potassium channel KCNO1 /DB_XREF=gi:1916294 /UG=Hs.79351 potassium channel, subfamily K, member 1 (TWIK-1) /FL=gb:U33632.1 gb:U90065.1 gb:U76996.1 gb:NM_002245.1	
nuclear receptor subfamily 3, group C, member 2	gb:NM_000901.1 /DEF=Homo sapiens nuclear receptor subfamily 3, group C, member 2 (NR3C2), mRNA. /FEA=mRNA /GEN=NR3C2 /PROD=nuclear receptor subfamily 3, group C, member 2 /DB_XREF=gi:4505198 /UG=Hs.1790 nuclear receptor subfamily 3, group C, member 2 /FL=gb:M16801.1 gb:NM_000901.1	205259_at
BTG family, member 2	gb:NM_006763.1 /DEF=Homo sapiens BTG family, member 2 (BTG2), mRNA. /FEA=mRNA /GEN=BTG2 /PROD=BTG family, member 2 /DB_XREF=gi:5802987 /UG=Hs.75462 BTG family, member 2 /FL=gb:U72649.1 gb:NM_006763.1	201236_s_at
G protein- coupled receptor 49	gb:AF062006.1 /DEF=Homo sapiens orphan G protein-coupled receptor HG38 mRNA, complete cds. /FEA=mRNA /PROD=orphan G protein-coupled receptor HG38 /DB_XREF=gi:3366801 /UG=Hs.285529 G protein-coupled receptor 49 /FL=gb:AF062006.1 gb:AF061444.1 gb:NM_003667.1	210393_at
hypothetical protein FLJ20048	gb:NM_017640.1 /DEF=Homo sapiens hypothetical protein FLJ20048 (FLJ20048), mRNA. /FEA=mRNA /GEN=FLJ20048 /PROD=hypothetical protein FLJ20048 /DB_XREF=gi:8923056 /UG=Hs.116470 hypothetical protein FLJ20048 /FL=gb:NM_017640.1	219573_at
cytochrome P450, subfamily III (arachidonic acid epoxygenase) polypeptide 2	gb:NM_000775.1 /DEF=Homo sapiens cytochrome P450, subfamily III (arachidonic acid epoxygenase) polypeptide 2 (CYP2J2), mRNA. /FEA=mRNA /GEN=CYP2J2 /PROD=cytochrome P450, subfamily III (arachidonic acid epoxygenase) polypeptide 2 /DB_XREF=gi:4503226 /UG=Hs.152096 cytochrome P450, subfamily III (arachidonic acid epoxygenase) polypeptide 2 /FL=gb:U37143.1 gb:NM_000775.1	205073_at
brain-specific protein p25 alpha	gb:NM_007030.1 /DEF=Homo sapiens brain- specific protein p25 alpha (p25), mRNA. /FEA=mRNA /GEN=p25 /PROD=brain-specific protein p25 alpha /DB_XREF=gi:5902017 /UG=Hs.29353 brain-specific protein p25 alpha	206179_s_at

	/FL=gb:AB017016.1 gb:NM_007030.1	
mucin 2, intestinal/trachea 1	gb:NM_002457.1 /DEF=Homo sapiens mucin 2, intestinaltracheal (MUC2), mRNA. /FEA=mRNA /GEN=MUC2 /PROD=mucin 2, intestinaltracheal /DB_XREF=gi:4505284 /UG=Hs.315 mucin 2, intestinaltracheal /FL=gb:NM_002457.1 gb:L21998.1	204673_at
hypothetical protein FLJ20174	gb:NM_017699.1 /DEF=Homo sapiens hypothetical protein FLJ20174 (FLJ20174), mRNA. /FEA=mRNA /GEN=FLJ20174 /PROD=hypothetical protein FLJ20174 /DB_XREF=gi:8923170 /UG=Hs.114556 hypothetical protein FLJ20174 /FL=gb:NM_017699.1	219734_at
metastasis- associated 1-like 1	gb:NM_004739.1 /DEF=Homo sapiens metastasis-associated 1-like 1 (MTA1L1), mRNA. /FEA=mRNA /GEN=MTA1L1 /PROD=metastasis-associated 1-like 1 /DB_XREF=gi:4758739 /UG=Hs.173043 metastasis-associated 1-like 1 /FL=gb:AB016591.1 gb:NM_004739.1 gb:AF295807.1	203444_s_at
bone morphogenetic protein 2	gb:NM_001200.1 /DEF=Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA. /FEA=mRNA /GEN=BMP2 /PROD=bone morphogenetic protein 2 precursor /DB_XREF=gi:4557368 /UG=Hs.73853 bone morphogenetic protein 2 /FL=gb:NM_001200.1	205290_s_at
heparanase	gb:NM_006665.1 /DEF=Homo sapiens heparanase (HPSE), mRNA. /FEA=mRNA /GEN=HPSE /PROD=heparanase /DB_XREF=gi:5729872 /UG=Hs.44227 heparanase /FL=gb:AF165154.1 gb:AF152376.1 gb:NM_006665.1 gb:AF084467.1 gb:AF155510.1	219403_s_at
tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator)	gb:BC002794.1 /DEF=Homo sapiens, tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator), clone MGC:3753, mRNA, complete cds. /FEA=mRNA /PROD=tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator) /DB_XREF=gi:12803894 /UG=Hs.279899 tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator) /FL=gb:BC002794.1 gb:U70321.1 gb:U81232.1 gb:NM_003820.1 gb:AF153978.1	209354_at
CUG triplet repeat, RNA-	Consensus includes gb:N36839 /FEA=EST /DB_XREF=gi:1157981	202156_s_at

binding protein 2	/DB_XREF=est:yy35f07.s1 /CLONE=IMAGE:273253 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:Nm_006561.1	
ESTs, Moderately similar to AF078844 1 hqp0376 protein [H.sapiens]	Consensus includes gb:R06655 /FEA=EST /DB_XREF=gi:757275 /DB_XREF=est:yf10e02.r1 /CLONE=IMAGE:126458 /UG=Hs.188518 ESTs, Moderately similar to AF078844 1 hqp0376 protein H.sapiens	217546_at
hairless (mouse) homolog	gb:Nm_018411.1 /DEF=Homo sapiens hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) (HSA277165), mRNA. /FEA=mRNA /GEN=HSA277165 /PROD=hairless protein /DB_XREF=gi:11036651 /UG=Hs.272367 hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) /FL=gb:Nm_018411.1	220163_s_at
branched chain aminotransferase 1, cytosolic	Consensus includes gb:Nm_005504.1 /DEF=Homo sapiens branched chain aminotransferase 1, cytosolic (BCAT1), mRNA. /FEA=CDS /GEN=BCAT1 /PROD=branched chain aminotransferase 1, cytosolic /DB_XREF=gi:5031606 /UG=Hs.157205 branched chain aminotransferase 1, cytosolic /FL=gb:U21551.1 gb:Nm_005504.1	214452_at
pancreas- enriched phospholipase C	gb:Nm_016341.1 /DEF=Homo sapiens pancreas-enriched phospholipase C (LOC51196), mRNA. /FEA=mRNA /GEN=LOC51196 /PROD=pancreas-enriched phospholipase C /DB_XREF=gi:7705940 /UG=Hs.6733 pancreas-enriched phospholipase C /FL=gb:AF190642.2 gb:AF117948.1 gb:Nm_016341.1	205112_at
prostaglandin- endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	gb:Nm_000963.1 /DEF=Homo sapiens prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) (PTGS2), mRNA. /FEA=mRNA /GEN=PTGS2 /PROD=prostaglandin-endoperoxide synthase 2(prostaglandin GH synthase and cyclooxygenase) /DB_XREF=gi:4506264 /UG=Hs.196384 prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and	204748_at

	cyclooxygenase) /FL=gb:M90100.1 gb:L15326.1 gb:NM_000963.1	
phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	gb:NM_000314.1 /DEF=Homo sapiens phosphatase and tensin homolog (mutated in multiple advanced cancers 1) (PTEN), mRNA. /FEA=mRNA /GEN=PTEN /PROD=phosphatase and tensin homolog (mutated in multiple advanced cancers 1) /DB_XREF=gi:4506248 /UG=Hs.10712 phosphatase and tensin homolog (mutated in multiple advanced cancers 1) /FL=gb:U92436.1 gb:U93051.1 gb:U96180.1 gb:NM_000314.1	204054_at
retinoic acid receptor responder (tazarotene induced) 1	Consensus includes gb:AI669229 /FEA=EST /DB_XREF=gi:4834003 /DB_XREF=est:wc13e06.x1 /CLONE=IMAGE:2315074 /UG=Hs.82547 retinoic acid receptor responder (tazarotene induced) 1	221872_at
protease inhibitor 3, skin-derived (SKALP)	gb:NM_002638.1 /DEF=Homo sapiens protease inhibitor 3, skin-derived (SKALP) (PI3), mRNA. /FEA=mRNA /GEN=PI3 /PROD=protease inhibitor 3, skin-derived (SKALP) /DB_XREF=gi:4505786 /UG=Hs.112341 protease inhibitor 3, skin-derived (SKALP) /FL=gb:NM_002638.1	203691_at
zinc finger protein 137 (clone pHZ-30)	gb:NM_003438.1 /DEF=Homo sapiens zinc finger protein 137 (clone pHZ-30) (ZNF137), mRNA. /FEA=mRNA /GEN=ZNF137 /PROD=zinc finger protein 137 (clone pHZ-30) /DB_XREF=gi:4507988 /UG=Hs.151689 zinc finger protein 137 (clone pHZ-30) /FL=gb:NM_003438.1 gb:U09414.1	207394_at
myosin, light polypeptide 5, regulatory	gb:NM_002477.1 /DEF=Homo sapiens myosin, light polypeptide 5, regulatory (MYL5), mRNA. /FEA=mRNA /GEN=MYL5 /PROD=myosin, light polypeptide 5, regulatory /DB_XREF=gi:4505304 /UG=Hs.170482 myosin, light polypeptide 5, regulatory /FL=gb:L03785.1 gb:NM_002477.1	205145_s_at
tumor necrosis factor receptor superfamily, member 6	gb:NM_000043.1 /DEF=Homo sapiens tumor necrosis factor receptor superfamily, member 6 (TNFRSF6), mRNA. /FEA=mRNA /GEN=TNFRSF6 /PROD=apoptosis (APO-1) antigen 1 /DB_XREF=gi:4507582 /UG=Hs.82359 tumor necrosis factor receptor superfamily, member 6 /FL=gb:M67454.1 gb:NM_000043.1	204781_s_at
hypothetical	Consensus includes gb:AI339568 /FEA=EST	222727_s_at

protein FLJ22233	/DB_XREF=gi:4076495 /DB_XREF=est:qk67e10.x1 /CLONE=IMAGE:1874058 /UG=Hs.286194 hypothetical protein FLJ22233 /FL=gb:NM_024959.1	
regenerating gene type IV	gb:AY007243.1 /DEF=Homo sapiens regenerating gene type IV mRNA, complete cds. /FEA=mRNA /PROD=regenerating gene type IV /DB_XREF=gi:12621025 /UG=Hs.105484 Homo sapiens regenerating gene type IV mRNA, complete cds /FL=gb:AY007243.1	223447_at
Homo sapiens cDNA: FLJ21962 fis, clone HEP05564	Consensus includes gb:AK025615.1 /DEF=Homo sapiens cDNA: FLJ21962 fis, clone HEP05564. /FEA=mRNA /DB_XREF=gi:10438186 /UG=Hs.7567 Homo sapiens cDNA: FLJ21962 fis, clone HEP05564	225285_at
phosphoprotein associated with glycosphingolipi d-enriched microdomains	Consensus includes gb:AK000680.1 /DEF=Homo sapiens cDNA FLJ20673 fis, clone KAlA4464. /FEA=mRNA /DB_XREF=gi:7020924 /UG=Hs.266175 phosphoprotein associated with GEMs /FL=gb:AF240634.1 gb:NM_018440.1	225626_at
hypothetical protein FLJ20209	Consensus includes gb:BF111925 /FEA=EST /DB_XREF=gi:10941704 /DB_XREF=est:7138g05.x1 /CLONE=IMAGE:3523784 /UG=Hs.3685 hypothetical protein FLJ20209	226171_at
Homo sapiens mRNA for KIAA1190 protein, partial cds	Consensus includes gb:AA532640 /FEA=EST /DB_XREF=gi:2276894 /DB_XREF=est:nj17c04.s1 /CLONE=IMAGE:986598 /UG=Hs.206259 Homo sapiens mRNA for KIAA1190 protein, partial cds	226484_at
KIAA1543 protein	Consensus includes gb:AB040976.1 /DEF=Homo sapiens mRNA for KIAA1543 protein, partial cds. /FEA=mRNA /GEN=KIAA1543 /PROD=KIAA1543 protein /DB_XREF=gi:7959352 /UG=Hs.17686 KIAA1543 protein	226494_at
hypothetical protein FLJ23563	Consensus includes gb:AW138767 /FEA=EST /DB_XREF=gi:6143085 /DB_XREF=est:UI-H- BI1-aep-a-12-0-UI.s1 /CLONE=IMAGE:2719799 /UG=Hs.274256 hypothetical protein FLJ23563	227180_at
ESTs	Consensus includes gb:AW264333 /FEA=EST /DB_XREF=gi:6641075 /DB_XREF=est:xq98e01.x1	227320_at

	/CLONE=IMAGE:2758680 /UG=Hs.21835 ESTs	
ESTs	Consensus includes gb:BF589359 /FEA=EST /DB_XREF=gi:11681683 /DB_XREF=est:nab25d01.x1 /CLONE=IMAGE:3266737 /UG=Hs.13256 ESTs	227354_at
Homo sapiens, Similar to RIKEN cDNA 1810037C20 gene, clone MGC:21481 IMAGE:385206 2, mRNA, complete cds	Consensus includes gb:AW001287 /FEA=EST /DB_XREF=gi:5848203 /DB_XREF=est:wu27e06.x1 /CLONE=IMAGE:2521282 /UG=Hs.61265 ESTs, Weakly similar to G786_HUMAN PROTEIN GS3786 H.sapiens	227676_at
Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	Consensus includes gb:T86159 /FEA=EST /DB_XREF=gi:714511 /DB_XREF=est:yd84h07.s1 /CLONE=IMAGE:114973 /UG=Hs.10450 Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	227724_at
ESTs	Consensus includes gb:AI700341 /FEA=EST /DB_XREF=gi:4988241 /DB_XREF=est:wd06e10.x1 /CLONE=IMAGE:2327370 /UG=Hs.110406 ESTs	228653_at
ESTs	Consensus includes gb:BG494007 /FEA=EST /DB_XREF=gi:13455521 /DB_XREF=est:602542289F1 /CLONE=IMAGE:4673182 /UG=Hs.203213 ESTs	228716_at
ESTs	Consensus includes gb:AI559300 /FEA=EST /DB_XREF=gi:4509505 /DB_XREF=est:tq43d03.x1 /CLONE=IMAGE:2211557 /UG=Hs.294140 ESTs	229331_at
hypothetical protein	Consensus includes gb:AI830823 /FEA=EST /DB_XREF=gi:5451416 /DB_XREF=est:wj52b06.x1 /CLONE=IMAGE:2406419 /UG=Hs.95549 hypothetical protein	229439_s_at
ESTs	Consensus includes gb:BF431989 /FEA=EST /DB_XREF=gi:11444103 /DB_XREF=est:nab84a05.x1 /CLONE=IMAGE:3274280 /UG=Hs.203213 ESTs	229657_at
ESTs	Consensus includes gb:BF589413 /FEA=EST	229893_at

	/DB_XREF=gi:11681737 /DB_XREF=est:nab26b11.x1 /CLONE=IMAGE:3267020 /UG=Hs.55501 ESTs	
brain-specific protein p25 alpha	Consensus includes gb:BG055052 /FEA=EST /DB_XREF=gi:12512386 /DB_XREF=est:nac94g06.x1 /CLONE=IMAGE:3441995 /UG=Hs.29353 brain-specific protein p25 alpha	230104_s_at
ESTs, Weakly similar to MMHUE4 erythrocyte membrane protein 4.1, parent splice form [H.sapiens]	Consensus includes gb:BF110588 /FEA=EST /DB_XREF=gi:10940278 /DB_XREF=est:7n39e12.x1 /CLONE=IMAGE:3567071 /UG=Hs.150478 ESTs, Weakly similar to KIAA0987 protein H.sapiens	230645_at
ESTs	Consensus includes gb:BF592062 /FEA=EST /DB_XREF=gi:11684386 /DB_XREF=est:7n98h06.x1 /CLONE=IMAGE:3572962 /UG=Hs.233890 ESTs	230760_at
hepatocyte nuclear factor 4, alpha	Consensus includes gb:AI032108 /FEA=EST /DB_XREF=gi:3250320 /DB_XREF=est:ow92d11.x1 /CLONE=IMAGE:1654293 /UG=Hs.54424 hepatocyte nuclear factor 4, alpha	230914_at
ESTs	Consensus includes gb:AW203959 /FEA=EST /DB_XREF=gi:6503431 /DB_XREF=est:UI-H- BI1-aeu-b-12-0-UI.s1 /CLONE=IMAGE:2720590 /UG=Hs.149532 ESTs	230944_at
ESTs	Consensus includes gb:AI139990 /FEA=EST /DB_XREF=gi:3647447 /DB_XREF=est:qa47d03.x1 /CLONE=IMAGE:1689893 /UG=Hs.134586 ESTs	231022_at
ESTs	Consensus includes gb:AI806131 /FEA=EST /DB_XREF=gi:5392697 /DB_XREF=est:wf06c06.x1 /CLONE=IMAGE:2349802 /UG=Hs.99376 ESTs	231148_at
hypothetical protein FLJ23045	Consensus includes gb:AB046810.1 /DEF=Homo sapiens mRNA for KIAA1590 protein, partial cds. /FEA=mRNA /GEN=KIAA1590 /PROD=KIAA1590 protein /DB_XREF=gi:10047254 /UG=Hs.101774 hypothetical protein FLJ23045	232083_at

Homo sapiens PAC clone RP5- 855D21	Consensus includes gb:AC004908 /DEF=Homo sapiens PAC clone RP5-855D21 /FEA=CDS_3 /DB_XREF=gi:4156179 /UG=Hs.249181 Homo sapiens PAC clone RP5-855D21	232641_at
putative microtubule- binding protein	Consensus includes gb:AJ251708.1 /DEF=Homo sapiens partial mRNA for putative microtubule-binding protein. /FEA=mRNA /PROD=putative microtubule-binding protein /DB_XREF=gi:6491740 /UG=Hs.326544 putative microtubule-binding protein	234669_x_at
ESTs	Consensus includes gb:AI741469 /FEA=EST /DB_XREF=gi:5109757 /DB_XREF=est:wgl1b01.x1 /CLONE=IMAGE:2364745 /UG=Hs.57787 ESTs	234970_at
ESTs	Consensus includes gb:AI417897 /FEA=EST /DB_XREF=gi:4261401 /DB_XREF=est:tg55b06.x1 /CLONE=IMAGE:2112659 /UG=Hs.235860 ESTs	235444_at
ESTs	Consensus includes gb:AI493909 /FEA=EST /DB_XREF=gi:4394912 /DB_XREF=est:qz94e02.x1 /CLONE=IMAGE:2042234 /UG=Hs.6131 ESTs	235562_at
ESTs	Consensus includes gb:AV741130 /FEA=EST /DB_XREF=gi:10858711 /DB_XREF=est:AV741130 /CLONE=CBCATB06 /UG=Hs.173704 ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens	235651_at
ESTs	Consensus includes gb:AW339510 /FEA=EST /DB_XREF=gi:6836136 /DB_XREF=est:xz91h08.x1 /CLONE=IMAGE:2871615 /UG=Hs.42722 ESTs	235866_at
ESTs	Consensus includes gb:AI076192 /FEA=EST /DB_XREF=gi:3405370 /DB_XREF=est:oz01g07.x1 /CLONE=IMAGE:1674108 /UG=Hs.131933 ESTs	236422_at
ESTs	Consensus includes gb:AL044570 /FEA=EST /DB_XREF=gi:5432785 /DB_XREF=est:DKFZp434L082_s1 /CLONE=DKFZp434L082 /UG=Hs.147975 ESTs	236548_at

ESTs	Consensus includes gb:AI733801 /FEA=EST /DB_XREF=gi:5054914 /DB_XREF=est:qk39c04.x5 /CLONE=IMAGE:1871334 /UG=Hs.146186 ESTs	237923_at
Homo sapiens, clone MGC:16402 IMAGE:394036 0, mRNA, complete cds	Consensus includes gb:T69015 /FEA=EST /DB_XREF=gi:680163 /DB_XREF=est:yc31f04.s1 /CLONE=IMAGE:82303 /UG=Hs.192728 ESTs	238422_at
ESTs	Consensus includes gb:AA502384 /FEA=EST /DB_XREF=gi:2237351 /DB_XREF=est:ne27f11.s1 /CLONE=IMAGE:898605 /UG=Hs.151529 ESTs	238956_at
ESTs	Consensus includes gb:AI739241 /FEA=EST /DB_XREF=gi:5101222 /DB_XREF=est:wi14h02.x1 /CLONE=IMAGE:2390259 /UG=Hs.171480 ESTs	238984_at
ESTs	Consensus includes gb:AA088446 /FEA=EST /DB_XREF=gi:1633958 /DB_XREF=est:zl89f04.s1 /CLONE=IMAGE:511807 /UG=Hs.170298 ESTs	239065_at
ESTs	Consensus includes gb:AI493046 /FEA=EST /DB_XREF=gi:4394049 /DB_XREF=est:qz49b04.x1 /CLONE=IMAGE:2030191 /UG=Hs.146133 ESTs	239148_at
ESTs	Consensus includes gb:AI243098 /FEA=EST /DB_XREF=gi:3838495 /DB_XREF=est:qh26e03.x1 /CLONE=IMAGE:1845820 /UG=Hs.178398 ESTs	239966_at
ESTs, Weakly similar to A49175 Motch B protein - mouse [M.musculus]	Consensus includes gb:AI633523 /FEA=EST /DB_XREF=gi:4684853 /DB_XREF=est:th68b11.x1 /CLONE=IMAGE:2123805 /UG=Hs.44705 ESTs	240106_at
betacellulin	Consensus includes gb:AI620677 /FEA=EST /DB_XREF=gi:4629803 /DB_XREF=est:tu85e09.x1 /CLONE=IMAGE:2257864 /UG=Hs.154191 ESTs	241412_at
ESTs	Consensus includes gb:BF696216 /FEA=EST /DB_XREF=gi:11981624	242626_at

	/DB_XREF=est:602124536F1 /CLONE=IMAGE:4281632 /UG=Hs.188724 ESTs	
ESTs	Consensus includes gb:N57929 /FEA=EST /DB_XREF=gi:1201819 /DB_XREF=est:yv61e06.s1 /CLONE=IMAGE:247234 /UG=Hs.48100 ESTs	242978_x_at
ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINAT ION WARNING ENTRY [H.sapiens]	Consensus includes gb:AI457984 /FEA=EST /DB_XREF=gi:4312002 /DB_XREF=est:tj66a04.x1 /CLONE=IMAGE:2146446 /UG=Hs.165900 ESTs, Weakly similar to ALUC_HUMAN !!!! ALU CLASS C WARNING ENTRY !!! H.sapiens	243729_at
ESTs	Consensus includes gb:AA581439 /FEA=EST /DB_XREF=gi:2359211 /DB_XREF=est:nh13c10.s1 /CLONE=IMAGE:952242 /UG=Hs.152328 ESTs	244650_at

The two biomarker probe sets A and B were then combined, a total of 161 different probe sets, and the redundant polynucleotides were removed, representing 125 unique polynucleotides which are provided below in Table 4. The Table 4

5 polynucleotides are biomarkers of the invention.

TABLE 4 - Biomarkers

Unigene Title And SEQ ID NO:	Affymetrix Description	Affymetrix probe set
3-hydroxy-3- methylglutaryl- Coenzyme A synthase 2 (mitochondrial) SEQ ID NOS: 1 (DNA) and 126 (amino acid)	gb:NM_005518.1 /DEF=Homo sapiens 3- hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) (HMGCS2), mRNA. /FEA=mRNA /GEN=HMGCS2 /PROD=3-hydroxy-3-methylglutaryl- Coenzyme A synthase 2(mitochondrial) /DB_XREF=gi:5031750 /UG=Hs.59889 3- hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /FL=gb:NM_005518.1	204607_at
ATPase, Class V, type 10B	Consensus includes gb:AW006935 /FEA=EST /DB_XREF=gi:5855713 /DB_XREF=est:wt08b11.x1	214070_s_at

SEQ ID NO: 2 (DNA)	/CLONE=IMAGE:2506845 /UG=Hs.109358 ATPase, Class V, type 10B	
bone morphogenetic protein 2 SEQ ID NOS: 3 (DNA) and 127 (amino acid)	gb:NM_001200.1 /DEF=Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA. /FEA=mRNA /GEN=BMP2 /PROD=bone morphogenetic protein 2 precursor /DB_XREF=gi:4557368 /UG=Hs.73853 bone morphogenetic protein 2 /FL=gb:NM_001200.1	205290_s_at
brain-specific protein p25 alpha SEQ ID NOS: 4 (DNA) and 128 (amino acid)	gb:NM_007030.1 /DEF=Homo sapiens brain- specific protein p25 alpha (p25), mRNA. /FEA=mRNA /GEN=p25 /PROD=brain- specific protein p25 alpha /DB_XREF=gi:5902017 /UG=Hs.29353 brain-specific protein p25 alpha /FL=gb:AB017016.1 gb:NM_007030.1	206179_s_at
branched chain aminotransferase 1, cytosolic SEQ ID NOS: 5 (DNA) and 129 (amino acid)	Consensus includes gb:NM_005504.1 /DEF=Homo sapiens branched chain aminotransferase 1, cytosolic (BCAT1), mRNA. /FEA=CDS /GEN=BCAT1 /PROD=branched chain aminotransferase 1, cytosolic /DB_XREF=gi:5031606 /UG=Hs.157205 branched chain aminotransferase 1, cytosolic /FL=gb:U21551.1 gb:NM_005504.1	214452_at
BTG family, member 2 SEQ ID NOS: 6 (DNA) and 130 (amino acid)	gb:NM_006763.1 /DEF=Homo sapiens BTG family, member 2 (BTG2), mRNA. /FEA=mRNA /GEN=BTG2 /PROD=BTG family, member 2 /DB_XREF=gi:5802987 /UG=Hs.75462 BTG family, member 2 /FL=gb:U72649.1 gb:NM_006763.1	201236_s_at
Carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) SEQ ID NOS: 7 (DNA) and 131 (amino acid)	gb:BC005008.1 /DEF=Homo sapiens, carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen), clone MGC:10467, mRNA, complete cds. /FEA=mRNA /PROD=carcinoembryonic antigen-related cell adhesionmolecule 6 (non-specific cross reacting antigen) /DB_XREF=gi:13477106 /UG=Hs.73848 carcinoembryonic antigen- related cell adhesion molecule 6 (non-specific cross reacting antigen) /FL=gb:BC005008.1 gb:M18216.1 gb:M29541.1 gb:NM_002483.1	203757_s_at
caspase 10, apoptosis- related cysteine protease SEQ ID NOS: 8	gb:NM_001230.1 /DEF=Homo sapiens caspase 10, apoptosis-related cysteine protease (CASP10), mRNA. /FEA=mRNA /GEN=CASP10 /PROD=caspase 10, apoptosis-related cysteine protease	205467_at

(DNA) and 132 (amino acid)	/DB_XREF=gi:4502568 /UG=Hs.5353 caspase 10, apoptosis-related cysteine protease /FL=gb:U60519.1 gb:Nm_001230.1	
CUG triplet repeat, RNA-binding protein 2 SEQ ID NOS: 9 (DNA) and 133 (amino acid)	gb:Nm_006561.1 /DEF=Homo sapiens CUG triplet repeat, RNA-binding protein 2 (CUGBP2), mRNA. /FEA=mRNA /GEN=CUGBP2 /PROD=CUG triplet repeat, RNA-binding protein 2 /DB_XREF=gi:5729815 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:Nm_006561.1	202158_s_at
cystatin S SEQ ID NOS: 10 (DNA) and 134 (amino acid)	gb:Nm_001899.1 /DEF=Homo sapiens cystatin S (CST4), mRNA. /FEA=mRNA /GEN=CST4 /PROD=cystatin S /DB_XREF=gi:4503108 /UG=Hs.56319 cystatin S /FL=gb:Nm_001899.1	206994_at
cystic fibrosis transmembrane conductance regulator, ATP- binding cassette (sub- family C, member 7) SEQ ID NOS: 11 (DNA) and 135 (amino acid)	gb:Nm_000492.2 /DEF=Homo sapiens cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) (CFTR), mRNA. /FEA=mRNA /GEN=CFTR /PROD=cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /DB_XREF=gi:6995995 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /FL=gb:Nm_000492.2	205043_at
cytochrome P450, subfamily IIIJ (arachidonic acid epoxygenase) polypeptide 2 SEQ ID NOS: 12 (DNA) and 136 (amino acid)	gb:Nm_000775.1 /DEF=Homo sapiens cytochrome P450, subfamily IIIJ (arachidonic acid epoxygenase) polypeptide 2 (CYP2J2), mRNA. /FEA=mRNA /GEN=CYP2J2 /PROD=cytochrome P450, subfamily IIIJ (arachidonic acid epoxygenase) polypeptide 2 /DB_XREF=gi:4503226 /UG=Hs.152096 cytochrome P450, subfamily IIIJ (arachidonic acid epoxygenase) polypeptide 2 /FL=gb:U37143.1 gb:Nm_000775.1	205073_at
dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) SEQ ID NOS 13 (DNA) and 137 (amino acid)	gb:M80536.1 /DEF=H.sapiens dipeptidyl peptidase IV (DPP4) mRNA, complete cds. /FEA=mRNA /GEN=DPP4 /PROD=dipeptidyl peptidase IV /DB_XREF=gi:181569 /UG=Hs.44926 dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) /FL=gb:M80536.1 gb:Nm_001935.1	203716_s_at
DKFZP434C091 protein	Consensus includes gb:AL080170.1 /DEF=Homo sapiens mRNA; cDNA	215047_at

SEQ ID NO: 14 (DNA)	DKFZp434C091 (from clone DKFZp434C091); partial cds. /FEA=mRNA /GEN=DKFZp434C091 /PROD=hypothetical protein /DB_XREF=gi:5262639 /UG=Hs.51692 DKFZP434C091 protein	
dopa decarboxylase (aromatic L-amino acid decarboxylase) SEQ ID NO: 15 (DNA)	Consensus includes gb:AW772056 /FEA=EST /DB_XREF=gi:7704118 /DB_XREF=est:hn64g06.x1 /CLONE=IMAGE:3032698 /UG=Hs.150403 dopa decarboxylase (aromatic L-amino acid decarboxylase)	214347_s_at
EphA1 SEQ ID NOS: 16 (DNA) and 138 (amino acid)	gb:NM_005232.1 /DEF=Homo sapiens EphA1 (EPHA1), mRNA. /FEA=mRNA /GEN=EPHA1 /PROD=EphA1 /DB_XREF=gi:4885208 /UG=Hs.89839 EphA1 /FL=gb:M18391.1 gb:NM_005232.1	205977_s_at
ESTs, Moderately similar to AF078844 1 hqp0376 protein [H.sapiens] SEQ ID NO: 17 (DNA)	Consensus includes gb:R06655 /FEA=EST /DB_XREF=gi:757275 /DB_XREF=est:yf10e02.r1 /CLONE=IMAGE:126458 /UG=Hs.188518 ESTs, Moderately similar to AF078844 1 hqp0376 protein H.sapiens	217546_at
ESTs, Weakly similar to I38022 hypothetical protein [H.sapiens] SEQ ID NO: 18 (DNA)	Consensus includes gb:AW675655 /FEA=EST /DB_XREF=gi:7540890 /DB_XREF=est:ba52e01.x1 /CLONE=IMAGE:2900184 /UG=Hs.314158 ESTs	222354_at
fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) SEQ ID NOS: 19 (DNA) and 139 (amino acid)	gb:NM_022969.1 /DEF=Homo sapiens fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2), transcript variant 2, mRNA. /FEA=mRNA /GEN=FGFR2 /PROD=fibroblast growth factor receptor 2, isoform 2precursor /DB_XREF=gi:13186252 /UG=Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) /FL=gb:NM_022969.1 gb:M97193.1 gb:M80634.1	203638_s_at
FXYP domain-containing ion	gb:BC005238.1 /DEF=Homo sapiens, FXYP domain-containing ion transport regulator 3,	202489_s_at

transport regulator 3 SEQ ID NOS: 20 (DNA) and 140 (amino acid)	clone MGC:12265, mRNA, complete cds. /FEA=mRNA /PROD=FXYP domain- containing ion transport regulator3 /DB_XREF=gi:13528881 /UG=Hs.301350 FXYP domain-containing ion transport regulator 3 /FL=gb:NM_005971.2 gb:BC005238.1	
G protein-coupled receptor 49 SEQ ID NOS: 21 (DNA) and 141 (amino acid)	gb:AF062006.1 /DEF=Homo sapiens orphan G protein-coupled receptor HG38 mRNA, complete cds. /FEA=mRNA /PROD=orphan G protein-coupled receptor HG38 /DB_XREF=gi:3366801 /UG=Hs.285529 G protein-coupled receptor 49 /FL=gb:AF062006.1 gb:AF061444.1 gb:NM_003667.1	210393_at
hairless (mouse) homolog SEQ ID NOS: 22 (DNA) and 142 (amino acid)	gb:NM_018411.1 /DEF=Homo sapiens hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) (HSA277165), mRNA. /FEA=mRNA /GEN=HSA277165 /PROD=hairless protein /DB_XREF=gi:11036651 /UG=Hs.272367 hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) /FL=gb:NM_018411.1	220163_s_at
hemoglobin, alpha 1 SEQ ID NOS: 23 (DNA) and 143 (amino acid)	gb:BC005931.1 /DEF=Homo sapiens, hemoglobin, alpha 2, clone MGC:14541, mRNA, complete cds. /FEA=mRNA /PROD=hemoglobin, alpha 2 /DB_XREF=gi:13543547 /FL=gb:BC005931.1	211745_x_at
hemoglobin, alpha 2 SEQ ID NO: 24 (DNA)	Consensus includes gb:T50399 /FEA=EST /DB_XREF=gi:652259 /DB_XREF=est:yb30b11.s1 /CLONE=IMAGE:72669 /UG=Hs.251577 hemoglobin, alpha 1	214414_x_at
heparanase SEQ ID NOS: 25 (DNA) and 144 (amino acid)	gb:NM_006665.1 /DEF=Homo sapiens heparanase (HPSE), mRNA. /FEA=mRNA /GEN=HPSE /PROD=heparanase /DB_XREF=gi:5729872 /UG=Hs.44227 heparanase /FL=gb:AF165154.1 gb:AF152376.1 gb:NM_006665.1 gb:AF084467.1 gb:AF155510.1	219403_s_at
Hermansky-Pudlak syndrome	Consensus includes gb:AL022313 /DEF=Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3	217354_s_at

SEQ ID NOS: 26 (DNA) and 145 (amino acid)	Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3-P66), the gene f... /FEA=CDS_3 /DB_XREF=gi:4200326 /UG=Hs.272270 Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3 Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3-P66), the gene for a nov	
HERV-H LTR- associating 2 SEQ ID NOS: 27 (DNA) and 146 (amino acid)	gb:NM_007072.1 /DEF=Homo sapiens HERV-H LTR-associating 2 (HHLA2), mRNA. /FEA=mRNA /GEN=HHLA2 /PROD=HERV-H LTR-associating 2 /DB_XREF=gi:5901963 /UG=Hs.252351 HERV-H LTR-associating 2 /FL=gb:AF126162.1 gb:NM_007072.1	220812_s_at
Homo sapiens clone 24707 mRNA sequence SEQ ID NO: 28 (DNA)	Consensus includes gb:AW593996 /FEA=EST /DB_XREF=gi:7281254 /DB_XREF=est:hg41g06.x1 /CLONE=IMAGE:2948218 /UG=Hs.124969 Homo sapiens clone 24707 mRNA sequence	213256_at
Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042) SEQ ID NO: 29 (DNA)	Consensus includes gb:AL049983.1 /DEF=Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042). /FEA=mRNA /DB_XREF=gi:4884234 /UG=Hs.240136 Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042)	217288_at
hypothetical protein FLJ20048 SEQ ID NOS: 30 (DNA) and 147 (amino acid)	gb:NM_017640.1 /DEF=Homo sapiens hypothetical protein FLJ20048 (FLJ20048), mRNA. /FEA=mRNA /GEN=FLJ20048 /PROD=hypothetical protein FLJ20048 /DB_XREF=gi:8923056 /UG=Hs.116470 hypothetical protein FLJ20048 /FL=gb:NM_017640.1	219573_at
hypothetical protein FLJ20075 SEQ ID NOS: 31 (DNA) and 148 (amino acid)	gb:NM_017655.1 /DEF=Homo sapiens hypothetical protein FLJ20075 (FLJ20075), mRNA. /FEA=mRNA /GEN=FLJ20075 /PROD=hypothetical protein FLJ20075 /DB_XREF=gi:8923083 /UG=Hs.205058 hypothetical protein FLJ20075 /FL=gb:NM_017655.1	219970_at

interferon consensus sequence binding protein 1 SEQ ID NO: 32 (DNA)	Consensus includes gb:AI073984 /FEA=EST /DB_XREF=gi:3400628 /DB_XREF=est:oy66c05.x1 /CLONE=IMAGE:1670792 /UG=Hs.14453 interferon consensus.sequence binding protein 1 /FL=gb:M91196.1 gb:NM_002163.1	204057_at
KIAA0690 protein SEQ ID NO: 33 (DNA)	Consensus includes gb:AK000238.1 /DEF=Homo sapiens cDNA FLJ20231 fis, clone COLF5511, highly similar to AB014590 Homo sapiens mRNA for KIAA0690 protein. /FEA=mRNA /DB_XREF=gi:7020188 /UG=Hs.60103 KIAA0690 protein	216360_x_at
matrilin 3 SEQ ID NOS: 34 (DNA) and 149 (amino acid)	gb:NM_002381.2 /DEF=Homo sapiens matrilin 3 (MATN3) precursor, mRNA. /FEA=mRNA /GEN=MATN3 /PROD=matrilin 3 precursor /DB_XREF=gi:13518040 /UG=Hs.278461 matrilin 3 /FL=gb:NM_002381.2	206091_at
metastasis-associated 1-like 1 SEQ ID NOS: 35 (DNA) and 150 (amino acid)	gb:NM_004739.1 /DEF=Homo sapiens metastasis-associated 1-like 1 (MTA1L1), mRNA. /FEA=mRNA /GEN=MTA1L1 /PROD=metastasis-associated 1-like 1 /DB_XREF=gi:4758739 /UG=Hs.173043 metastasis-associated 1-like 1 /FL=gb:AB016591.1 gb:NM_004739.1 gb:AF295807.1	203444_s_at
mucin 2, intestinal/tracheal SEQ ID NOS: 36 (DNA) and 151 (amino acid)	gb:NM_002457.1 /DEF=Homo sapiens mucin 2, intestinaltracheal (MUC2), mRNA. /FEA=mRNA /GEN=MUC2 /PROD=mucin 2, intestinaltracheal /DB_XREF=gi:4505284 /UG=Hs.315 mucin 2, intestinaltracheal /FL=gb:NM_002457.1 gb:L21998.1	204673_at
mucin 3B SEQ ID NOS: 37 (DNA) and 152 (amino acid)	Consensus includes gb:AB038783.1 /DEF=Homo sapiens MUC3B mRNA for intestinal mucin, partial cds. /FEA=mRNA /GEN=MUC3B /PROD=intestinal mucin /DB_XREF=gi:9929917 /UG=Hs.129782 mucin 3A, intestinal	214898_x_at
myosin, heavy polypeptide 13, skeletal muscle SEQ ID NOS: 38 (DNA) and 153 (amino acid)	gb:NM_003802.1 /DEF=Homo sapiens myosin, heavy polypeptide 13, skeletal muscle (MYH13), mRNA. /FEA=mRNA /GEN=MYH13 /PROD=myosin, heavy polypeptide 13, skeletal muscle /DB_XREF=gi:11321578 /UG=Hs.278488 myosin, heavy polypeptide 13, skeletal muscle /FL=gb:NM_003802.1 gb:AF111782.2	208208_at

myosin, light polypeptide 5, regulatory SEQ ID NOS: 39 (DNA) and 154 (amino acid)	gb:NM_002477.1 /DEF=Homo sapiens myosin, light polypeptide 5, regulatory (MYL5), mRNA. /FEA=mRNA /GEN=MYL5 /PROD=myosin, light polypeptide 5, regulatory /DB_XREF=gi:4505304 /UG=Hs.170482 myosin, light polypeptide 5, regulatory /FL=gb:L03785.1 gb:NM_002477.1	205145_s_at
nuclear receptor subfamily 3, group C, member 2 SEQ ID NOS: 40 (DNA) and 155 (amino acid)	gb:NM_000901.1 /DEF=Homo sapiens nuclear receptor subfamily 3, group C, member 2 (NR3C2), mRNA. /FEA=mRNA /GEN=NR3C2 /PROD=nuclear receptor subfamily 3, group C, member 2 /DB_XREF=gi:4505198 /UG=Hs.1790 nuclear receptor subfamily 3, group C, member 2 /FL=gb:M16801.1 gb:NM_000901.1	205259_at
nuclear receptor subfamily 5, group A, member 2 SEQ ID NOS: 41 (DNA) and 156 (amino acid)	Consensus includes gb:AF228413.1 /DEF=Homo sapiens hepatocyte transcription factor mRNA, 3UTR. /FEA=mRNA /DB_XREF=gi:7677372 /UG=Hs.183123 nuclear receptor subfamily 5, group A, member 2 /FL=gb:U93553.1 gb:AB019246.1 gb:AF124247.1	210174_at
pancreas-enriched phospholipase C SEQ ID NOS: 42 (DNA) and 157 (amino acid)	gb:NM_016341.1 /DEF=Homo sapiens pancreas-enriched phospholipase C (LOC51196), mRNA. /FEA=mRNA /GEN=LOC51196 /PROD=pancreas-enriched phospholipase C /DB_XREF=gi:7705940 /UG=Hs.6733 pancreas-enriched phospholipase C /FL=gb:AF190642.2 gb:AF117948.1 gb:NM_016341.1	205112_at
peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase SEQ ID NOS: 43 (DNA) and 158 (amino acid)	gb:NM_018441.1 /DEF=Homo sapiens peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase (HSA250303), mRNA. /FEA=mRNA /GEN=HSA250303 /PROD=peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase /DB_XREF=gi:8923751 /UG=Hs.281680 peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase /FL=gb:NM_018441.1	221142_s_at
phosducin SEQ ID NOS: 44 (DNA) and 159 (amino acid)	gb:M33478.1 /DEF=Human 33-kDa phototransducing protein mRNA, complete cds. /FEA=mRNA /DB_XREF=gi:177186 /UG=Hs.550 phosducin /FL=gb:NM_022577.1 gb:M33478.1	211496_s_at

	gb:AF076465.1	
phosphatase and tensin homolog (mutated in multiple advanced cancers 1) SEQ ID NOS: 45 (DNA) and 160 (amino acid)	gb:NM_000314.1 /DEF=Homo sapiens phosphatase and tensin homolog (mutated in multiple advanced cancers 1) (PTEN), mRNA. /FEA=mRNA /GEN=PTEN /PROD=phosphatase and tensin homolog (mutated in multiple advanced cancers 1) /DB_XREF=gi:4506248 /UG=Hs.10712 phosphatase and tensin homolog (mutated in multiple advanced cancers 1) /FL=gb:U92436.1 gb:U93051.1 gb:U96180.1 gb:NM_000314.1	204054_at
potassium channel, subfamily K, member 1 (TWIK-1) SEQ ID NOS: 46 (DNA) and 161 (amino acid)	gb:U90065.1 /DEF=Human potassium channel KCNO1 mRNA, complete cds. /FEA=mRNA /PROD=potassium channel KCNO1 /DB_XREF=gi:1916294 /UG=Hs.79351 potassium channel, subfamily K, member 1 (TWIK-1) /FL=gb:U33632.1 gb:U90065.1 gb:U76996.1 gb:NM_002245.1	204678_s_at
prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) SEQ ID NOS: 47 (DNA) and 162 (amino acid)	gb:NM_000963.1 /DEF=Homo sapiens prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) (PTGS2), mRNA. /FEA=mRNA /GEN=PTGS2 /PROD=prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) /DB_XREF=gi:4506264 /UG=Hs.196384 prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) /FL=gb:M90100.1 gb:L15326.1 gb:NM_000963.1	204748_at
protease inhibitor 3, skin-derived (SKALP) SEQ ID NOS: 48 (DNA) and 163 (amino acid)	gb:NM_002638.1 /DEF=Homo sapiens protease inhibitor 3, skin-derived (SKALP) (PI3), mRNA. /FEA=mRNA /GEN=PI3 /PROD=protease inhibitor 3, skin-derived (SKALP) /DB_XREF=gi:4505786 /UG=Hs.112341 protease inhibitor 3, skin-derived (SKALP) /FL=gb:NM_002638.1	203691_at
PTPRF interacting protein, binding protein 2 (liprin beta 2) SEQ ID NO: 49 (DNA)	Consensus includes gb:AI692180 /FEA=EST /DB_XREF=gi:4969520 /DB_XREF=est:wd37f06.x1 /CLONE=IMAGE:2330339 /UG=Hs.12953 PTPRF interacting protein, binding protein 2 (liprin beta 2)	212841_s_at
retinoic acid receptor responder (tazarotene induced) 1	Consensus includes gb:AI669229 /FEA=EST /DB_XREF=gi:4834003 /DB_XREF=est:wc13e06.x1	221872_at

SEQ ID NO: 50 (DNA)	/CLONE=IMAGE:2315074 /UG=Hs.82547 retinoic acid receptor responder (tazarotene induced) 1	
Rho GTPase activating protein 8 SEQ ID NOS: 51 (DNA) and 164 (amino acid)	gb:NM_015366.1 /DEF=Homo sapiens Rho GTPase activating protein 8 (ARHGAP8), mRNA. /FEA=mRNA /GEN=ARHGAP8 /PROD=Rho GTPase activating protein 8 /DB_XREF=gi:7656903 /UG=Hs.102336 Rho GTPase activating protein 8 /FL=gb:NM_015366.1	205980_s_at
ribonuclease, RNase A family, 1 (pancreatic) SEQ ID NOS: 52 (DNA) and 165 (amino acid)	gb:NM_002933.1 /DEF=Homo sapiens ribonuclease, RNase A family, 1 (pancreatic) (RNASE1), mRNA. /FEA=mRNA /GEN=RNASE1 /PROD=ribonuclease, RNase A family, 1 (pancreatic) /DB_XREF=gi:4506546 /UG=Hs.78224 ribonuclease, RNase A family, 1 (pancreatic) /FL=gb:BC005324.1 gb:NM_002933.1 gb:D26129.1	201785_at
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 SEQ ID NOS: 53 (DNA) and 166 (amino acid)	gb:NM_002639.1 /DEF=Homo sapiens serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5), mRNA. /FEA=mRNA /GEN=SERPINB5 /PROD=serine (or cysteine) proteinase inhibitor, cladeB (ovalbumin), member 5 /DB_XREF=gi:4505788 /UG=Hs.55279 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 /FL=gb:NM_002639.1 gb:U04313.1	204855_at
spondin 1, (f-spondin) extracellular matrix protein SEQ ID NO: 54 (DNA)	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:w192a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213994_s_at
superoxide dismutase 3, extracellular SEQ ID NOS: 55 (DNA) and 167 (amino acid)	gb:NM_003102.1 /DEF=Homo sapiens superoxide dismutase 3, extracellular (SOD3), mRNA. /FEA=mRNA /GEN=SOD3 /PROD=superoxide dismutase 3, extracellular /DB_XREF=gi:4507150 /UG=Hs.2420 superoxide dismutase 3, extracellular /FL=gb:J02947.1 gb:NM_003102.1	205236_x_at
tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator)	gb:BC002794.1 /DEF=Homo sapiens, tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator), clone MGC:3753, mRNA, complete cds. /FEA=mRNA /PROD=tumor necrosis factor receptor superfamily, member 14 (herpesvirus	209354_at

SEQ ID NOS: 56 (DNA) and 168 (amino acid)	entry mediator) /DB_XREF=gi:12803894 /UG=Hs.279899 tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator) /FL=gb:BC002794.1 gb:U70321.1 gb:U81232.1 gb:NM_003820.1 gb:AF153978.1	
tumor necrosis factor receptor superfamily, member 6 SEQ ID NOS: 57 (DNA) and 169 (amino acid)	gb:NM_000043.1 /DEF=Homo sapiens tumor necrosis factor receptor superfamily, member 6 (TNFRSF6), mRNA. /FEA=mRNA /GEN=TNFRSF6 /PROD=apoptosis (APO-1) antigen 1 /DB_XREF=gi:4507582 /UG=Hs.82359 tumor necrosis factor receptor superfamily, member 6 /FL=gb:M67454.1 gb:NM_000043.1	204781_s_at
zinc finger protein 137 (clone pHZ-30) SEQ ID NOS: 58 (DNA) and 170 (amino acid)	gb:NM_003438.1 /DEF=Homo sapiens zinc finger protein 137 (clone pHZ-30) (ZNF137), mRNA. /FEA=mRNA /GEN=ZNF137 /PROD=zinc finger protein 137 (clone pHZ- 30) /DB_XREF=gi:4507988 /UG=Hs.151689 zinc finger protein 137 (clone pHZ-30) /FL=gb:NM_003438.1 gb:U09414.1	207394_at
hypothetical protein FLJ22233 SEQ ID NO: 59 (DNA)	Consensus includes gb:AI339568 /FEA=EST /DB_XREF=gi:4076495 /DB_XREF=est:qk67e10.x1 /CLONE=IMAGE:1874058 /UG=Hs.286194 hypothetical protein FLJ22233 /FL=gb:NM_024959.1	222727_s_at
regenerating gene type IV SEQ ID NOS: 60 (DNA) and 171 (amino acid)	gb:AY007243.1 /DEF=Homo sapiens regenerating gene type IV mRNA, complete cds. /FEA=mRNA /PROD=regenerating gene type IV /DB_XREF=gi:12621025 /UG=Hs.105484 Homo sapiens regenerating gene type IV mRNA, complete cds /FL=gb:AY007243.1	223447_at
Homo sapiens cDNA: FLJ21962 fis, clone HEP05564 SEQ ID NO: 61 (DNA)	Consensus includes gb:AK025615.1 /DEF=Homo sapiens cDNA: FLJ21962 fis, clone HEP05564. /FEA=mRNA /DB_XREF=gi:10438186 /UG=Hs.7567 Homo sapiens cDNA: FLJ21962 fis, clone HEP05564	225285_at
ESTs SEQ ID NO: 62 (DNA)	Consensus includes gb:N37023 /FEA=EST /DB_XREF=gi:1158165 /DB_XREF=est:yy40d03.s1 /CLONE=IMAGE:273701 /UG=Hs.235883 ESTs	225407_at
phosphoprotein associated with glycosphingolipid-	Consensus includes gb:AK000680.1 /DEF=Homo sapiens cDNA FLJ20673 fis, clone KAIA4464. /FEA=mRNA	225626_at

enriched microdomains SEQ ID NOS: 63 (DNA) and 172 (amino acid)	/DB_XREF=gi:7020924 /UG=Hs.266175 phosphoprotein associated with GEMs /FL=gb:AF240634.1 gb:NM_018440.1	
prostate cancer associated protein 7 SEQ ID NO: 64 (DNA)	Consensus includes gb:AA633076 /FEA=EST /DB_XREF=gi:2556490 /DB_XREF=est:nq38a06.s1 /CLONE=IMAGE:1146130 /UG=Hs.27495 prostate cancer associated protein 7	226167_at
Homo sapiens, Similar to RIKEN cDNA 1110060018 gene, clone MGC:17236 IMAGE:3864137, mRNA, complete cds SEQ ID NO: 65 (DNA)	Consensus includes gb:AA524690 /FEA=EST /DB_XREF=gi:2265618 /DB_XREF=est:ng38e07.s1 /CLONE=IMAGE:937092 /UG=Hs.294143 ESTs, Weakly similar to predicted using Genefinder C.elegans	226168_at
hypothetical protein FLJ20209 SEQ ID NO: 66 (DNA)	Consensus includes gb:BF111925 /FEA=EST /DB_XREF=gi:10941704 /DB_XREF=est:7138g05.x1 /CLONE=IMAGE:3523784 /UG=Hs.3685 hypothetical protein FLJ20209	226171_at
Homo sapiens mRNA for KIAA1190 protein, partial cds SEQ ID NOS: 67 (DNA) and 173 (amino acid)	Consensus includes gb:AA532640 /FEA=EST /DB_XREF=gi:2276894 /DB_XREF=est:nj17c04.s1 /CLONE=IMAGE:986598 /UG=Hs.206259 Homo sapiens mRNA for KIAA1190 protein, partial cds	226484_at
KIAA1543 protein SEQ ID NOS: 68 (DNA) and 174 (amino acid)	Consensus includes gb:AB040976.1 /DEF=Homo sapiens mRNA for KIAA1543 protein, partial cds. /FEA=mRNA /GEN=KIAA1543 /PROD=KIAA1543 protein /DB_XREF=gi:7959352 /UG=Hs.17686 KIAA1543 protein	226494_at
hypothetical protein MGC20702 SEQ ID NO: 69 (DNA)	Consensus includes gb:AK002203.1 /DEF=Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786. /FEA=mRNA /DB_XREF=gi:7023932 /UG=Hs.10260 Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786	226992_at
Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	Consensus includes gb:AA129774 /FEA=EST /DB_XREF=gi:1690185 /DB_XREF=est:zl16h09.s1	227019_at

SEQ ID NO: 70 (DNA)	/CLONE=IMAGE:502145 /UG=Hs.288905 Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	
hypothetical protein FLJ23563 SEQ ID NO: 71 (DNA)	Consensus includes gb:AW138767 /FEA=EST /DB_XREF=gi:6143085 /DB_XREF=est:UI-H-BI1-aep-a-12-0-UI.s1 /CLONE=IMAGE:2719799 /UG=Hs.274256 hypothetical protein FLJ23563	227180_at
ESTs SEQ ID NO: 72 (DNA)	Consensus includes gb:AW264333 /FEA=EST /DB_XREF=gi:6641075 /DB_XREF=est:xq98e01.x1 /CLONE=IMAGE:2758680 /UG=Hs.21835 ESTs	227320_at
ESTs SEQ ID NO: 73 (DNA)	Consensus includes gb:BF589359 /FEA=EST /DB_XREF=gi:11681683 /DB_XREF=est:nab25d01.x1 /CLONE=IMAGE:3266737 /UG=Hs.13256 ESTs	227354_at
Homo sapiens, Similar to RIKEN cDNA 1810037C20 gene, clone MGC:21481 IMAGE:3852062, mRNA, complete cds SEQ ID NO: 74 (DNA)	Consensus includes gb:AW001287 /FEA=EST /DB_XREF=gi:5848203 /DB_XREF=est:wu27e06.x1 /CLONE=IMAGE:2521282 /UG=Hs.61265 ESTs, Weakly similar to G786_HUMAN PROTEIN GS3786 H.sapiens	227676_at
ESTs, Weakly similar to JX0331 laurate omega-hydroxylase [H.sapiens] SEQ ID NO: 75 (DNA)	Consensus includes gb:AA557324 /FEA=EST /DB_XREF=gi:2327801 /DB_XREF=est:nl81a02.s1 /CLONE=IMAGE:1057034 /UG=Hs.26040 ESTs, Weakly similar to fatty acid omega- hydroxylase H.sapiens	227702_at
Homo sapiens cDNA: FLJ22063 fis, clone HEP10326 SEQ ID NO: 76 (DNA)	Consensus includes gb:T86159 /FEA=EST /DB_XREF=gi:714511 /DB_XREF=est:yd84h07.s1 /CLONE=IMAGE:114973 /UG=Hs.10450 Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	227724_at
GalNAc alpha-2, 6- sialyltransferase I, long form SEQ ID NOS: 77 (DNA) and 175 (amino acid)	Consensus includes gb:Y11339.2 /DEF=Homo sapiens mRNA for GalNAc alpha-2, 6-sialyltransferase I, long form. /FEA=mRNA /PROD=GalNAc alpha-2,6- sialyltransferase I /DB_XREF=gi:7576275 /UG=Hs.105352 GalNAc alpha-2, 6- sialyltransferase I, long form	227725_at

ESTs, Weakly similar to JE0350 Anterior gradient-2 [H.sapiens] SEQ ID NO: 78 (DNA)	Consensus includes gb:AI827789 /FEA=EST /DB_XREF=gi:5448449 /DB_XREF=est:wf33a07.x1 /CLONE=IMAGE:2357364 /UG=Hs.100686 ESTs, Weakly similar to JE0350 Anterior gradient-2 H.sapiens	228241_at
ESTs SEQ ID NO: 79 (DNA)	Consensus includes gb:AI700341 /FEA=EST /DB_XREF=gi:4988241 /DB_XREF=est:wd06e10.x1 /CLONE=IMAGE:2327370 /UG=Hs.110406 ESTs	228653_at
ESTs SEQ ID NO: 80 (DNA)	Consensus includes gb:BG494007 /FEA=EST /DB_XREF=gi:13455521 /DB_XREF=est:602542289F1 /CLONE=IMAGE:4673182 /UG=Hs.203213 ESTs	228716_at
anterior gradient 2 (Xenopus laevis) homolog SEQ ID NO: 81 (DNA)	Consensus includes gb:AI922323 /FEA=EST /DB_XREF=gi:5658287 /DB_XREF=est:wn90h03.x1 /CLONE=IMAGE:2453141 /UG=Hs.293380 ESTs	228969_at
Homo sapiens cDNA: FLJ23331 fis, clone HEP12664 SEQ ID NO: 82 (DNA)	Consensus includes gb:AK026984.1 /DEF=Homo sapiens cDNA: FLJ23331 fis, clone HEP12664. /FEA=mRNA /DB_XREF=gi:10439980 /UG=Hs.50742 Homo sapiens cDNA: FLJ23331 fis, clone HEP12664	229021_at
ESTs SEQ ID NO: 83 (DNA)	Consensus includes gb:AI559300 /FEA=EST /DB_XREF=gi:4509505 /DB_XREF=est:tq43d03.x1 /CLONE=IMAGE:2211557 /UG=Hs.294140 ESTs	229331_at
hypothetical protein SEQ ID NO: 84 (DNA)	Consensus includes gb:AI830823 /FEA=EST /DB_XREF=gi:5451416 /DB_XREF=est:wj52b06.x1 /CLONE=IMAGE:2406419 /UG=Hs.95549 hypothetical protein	229439_s_at
ESTs SEQ ID NO: 85 (DNA)	Consensus includes gb:BF431989 /FEA=EST /DB_XREF=gi:11444103 /DB_XREF=est:nab84a05.x1 /CLONE=IMAGE:3274280 /UG=Hs.203213 ESTs	229657_at
ESTs SEQ ID NO: 86 (DNA)	Consensus includes gb:BF589413 /FEA=EST /DB_XREF=gi:11681737 /DB_XREF=est:nab26b11.x1 /CLONE=IMAGE:3267020 /UG=Hs.55501	229893_at

	ESTs	
brain-specific protein p25 alpha SEQ ID NO: 87 (DNA)	Consensus includes gb:BG055052 /FEA=EST /DB_XREF=gi:12512386 /DB_XREF=est:nac94g06.x1 /CLONE=IMAGE:3441995 /UG=Hs.29353 brain-specific protein p25 alpha	230104_s_at
ESTs, Weakly similar to MMHUE4 erythrocyte membrane protein 4.1, parent splice form [H.sapiens] SEQ ID NO: 88 (DNA)	Consensus includes gb:BF110588 /FEA=EST /DB_XREF=gi:10940278 /DB_XREF=est:7n39e12.x1 /CLONE=IMAGE:3567071 /UG=Hs.150478 ESTs, Weakly similar to KIAA0987 protein H.sapiens	230645_at
ESTs SEQ ID NO: 89 (DNA)	Consensus includes gb:BF592062 /FEA=EST /DB_XREF=gi:11684386 /DB_XREF=est:7n98h06.x1 /CLONE=IMAGE:3572962 /UG=Hs.233890 ESTs	230760_at
hepatocyte nuclear factor 4, alpha SEQ ID NO: 90 (DNA)	Consensus includes gb:AI032108 /FEA=EST /DB_XREF=gi:3250320 /DB_XREF=est:ow92d11.x1 /CLONE=IMAGE:1654293 /UG=Hs.54424 hepatocyte nuclear factor 4, alpha	230914_at
ESTs SEQ ID NO: 91 (DNA)	Consensus includes gb:AW203959 /FEA=EST /DB_XREF=gi:6503431 /DB_XREF=est:UI-H-BI1-aeu-b-12-0-UI.s1 /CLONE=IMAGE:2720590 /UG=Hs.149532 ESTs	230944_at
ESTs SEQ ID NO: 92 (DNA)	Consensus includes gb:AI139990 /FEA=EST /DB_XREF=gi:3647447 /DB_XREF=est:qa47d03.x1 /CLONE=IMAGE:1689893 /UG=Hs.134586 ESTs	231022_at
ESTs SEQ ID NO: 93 (DNA)	Consensus includes gb:AI806131 /FEA=EST /DB_XREF=gi:5392697 /DB_XREF=est:wf06c06.x1 /CLONE=IMAGE:2349802 /UG=Hs.99376 ESTs	231148_at
hypothetical protein FLJ23045 SEQ ID NO: 94 (DNA)	Consensus includes gb:AB046810.1 /DEF=Homo sapiens mRNA for KIAA1590 protein, partial cds. /FEA=mRNA /GEN=KIAA1590 /PROD=KIAA1590 protein /DB_XREF=gi:10047254 /UG=Hs.101774 hypothetical protein FLJ23045	232083_at
Homo sapiens cDNA:	Consensus includes gb:AK026404.1	232321_at

FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA SEQ ID NO: 95 (DNA)	/DEF=Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA. /FEA=mRNA /DB_XREF=gi:10439257 /UG=Hs.271819 Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA	
Homo sapiens PAC clone RP5-855D21 SEQ ID NOS: 96 (DNA), 176 (amino acid), 177 (amino acid), and 178 (amino acid)	Consensus includes gb:AC004908 /DEF=Homo sapiens PAC clone RP5- 855D21 /FEA=CDS_3 /DB_XREF=gi:4156179 /UG=Hs.249181 Homo sapiens PAC clone RP5-855D21	232641_at
putative microtubule- binding protein SEQ ID NO: 97 (DNA)	Consensus includes gb:AJ251708.1 /DEF=Homo sapiens partial mRNA for putative microtubule-binding protein. /FEA=mRNA /PROD=putative microtubule- binding protein /DB_XREF=gi:6491740 /UG=Hs.326544 putative microtubule-binding protein	234669_x_at
ESTs SEQ ID NO: 98 (DNA)	Consensus includes gb:AI741469 /FEA=EST /DB_XREF=gi:5109757 /DB_XREF=est:wg11b01.x1 /CLONE=IMAGE:2364745 /UG=Hs.57787 ESTs	234970_at
ESTs SEQ ID NO: 99 (DNA)	Consensus includes gb:AI417897 /FEA=EST /DB_XREF=gi:4261401 /DB_XREF=est:tg55b06.x1 /CLONE=IMAGE:2112659 /UG=Hs.235860 ESTs	235444_at
ESTs SEQ ID NO: 100 (DNA)	Consensus includes gb:AA827649 /FEA=EST /DB_XREF=gi:2900090 /DB_XREF=est:od01a12.s1 /CLONE=IMAGE:1357918 /UG=Hs.105317 ESTs	235515_at
ESTs SEQ ID NO: 101 (DNA)	Consensus includes gb:AI493909 /FEA=EST /DB_XREF=gi:4394912 /DB_XREF=est:qz94e02.x1 /CLONE=IMAGE:2042234 /UG=Hs.6131 ESTs	235562_at
ESTs SEQ ID NO: 102 (DNA)	Consensus includes gb:AV741130 /FEA=EST /DB_XREF=gi:10858711 /DB_XREF=est:AV741130 /CLONE=CBCATB06 /UG=Hs.173704	235651_at

	ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens	
ESTs, Weakly similar to I38588 reverse transcriptase homolog [H.sapiens] SEQ ID NO: 103 (DNA)	Consensus includes gb:AI864053 /FEA=EST /DB_XREF=gi:5528160 /DB_XREF=est:wj55h10.x1 /CLONE=IMAGE:2406787 /UG=Hs.39972 ESTs, Weakly similar to I38588 reverse transcriptase homolog H.sapiens	235678_at
ESTs SEQ ID NO: 104 (DNA)	Consensus includes gb:AW339510 /FEA=EST /DB_XREF=gi:6836136 /DB_XREF=est:xz91h08.x1 /CLONE=IMAGE:2871615 /UG=Hs.42722 ESTs	235866_at
ESTs SEQ ID NO: 105 (DNA)	Consensus includes gb:AI076192 /FEA=EST /DB_XREF=gi:3405370 /DB_XREF=est:oz01g07.x1 /CLONE=IMAGE:1674108 /UG=Hs.131933 ESTs	236422_at
ESTs SEQ ID NO: 106 (DNA)	Consensus includes gb:AL044570 /FEA=EST /DB_XREF=gi:5432785 /DB_XREF=est:DKFZp434L082_s1 /CLONE=DKFZp434L082 /UG=Hs.147975 ESTs	236548_at
ESTs SEQ ID NO: 107 (DNA)	Consensus includes gb:AI968097 /FEA=EST /DB_XREF=gi:5764915 /DB_XREF=est:wul3a12.x1 /CLONE=IMAGE:2516830 /UG=Hs.131360 ESTs	237835_at
ESTs SEQ ID NO: 108 (DNA)	Consensus includes gb:AI733801 /FEA=EST /DB_XREF=gi:5054914 /DB_XREF=est:qk39c04.x5 /CLONE=IMAGE:1871334 /UG=Hs.146186 ESTs	237923_at
ESTs SEQ ID NO: 109 (DNA)	Consensus includes gb:BF594323 /FEA=EST /DB_XREF=gi:11686647 /DB_XREF=est:7h79g07.x1 /CLONE=IMAGE:3322236 /UG=Hs.158989 ESTs	238103_at
Homo sapiens, clone MGC:16402 IMAGE:3940360, mRNA, complete cds SEQ ID NO: 110 (DNA)	Consensus includes gb:T69015 /FEA=EST /DB_XREF=gi:680163 /DB_XREF=est:yc31f04.s1 /CLONE=IMAGE:82303 /UG=Hs.192728 ESTs	238422_at

ESTs SEQ ID NO: 111 (DNA)	Consensus includes gb:AA502384 /FEA=EST /DB_XREF=gi:2237351 /DB_XREF=est:ne27f11.s1 /CLONE=IMAGE:898605 /UG=Hs.151529 ESTs	238956_at
ESTs SEQ ID NO: 112 (DNA)	Consensus includes gb:AI739241 /FEA=EST /DB_XREF=gi:5101222 /DB_XREF=est:wi14h02.x1 /CLONE=IMAGE:2390259 /UG=Hs.171480 ESTs	238984_at
ESTs SEQ ID NO: 113 (DNA)	Consensus includes gb:AA088446 /FEA=EST /DB_XREF=gi:1633958 /DB_XREF=est:zl89f04.s1 /CLONE=IMAGE:511807 /UG=Hs.170298 ESTs	239065_at
ESTs SEQ ID NO: 114 (DNA)	Consensus includes gb:AI493046 /FEA=EST /DB_XREF=gi:4394049 /DB_XREF=est:qz49b04.x1 /CLONE=IMAGE:2030191 /UG=Hs.146133 ESTs	239148_at
ESTs SEQ ID NO: 115 (DNA)	Consensus includes gb:AI243098 /FEA=EST /DB_XREF=gi:3838495 /DB_XREF=est:qh26e03.x1 /CLONE=IMAGE:1845820 /UG=Hs.178398 ESTs	239966_at
ESTs, Weakly similar to A49175 Motch B protein - mouse [M.musculus] SEQ ID NO: 116 (DNA)	Consensus includes gb:AI633523 /FEA=EST /DB_XREF=gi:4684853 /DB_XREF=est:th68b11.x1 /CLONE=IMAGE:2123805 /UG=Hs.44705 ESTs	240106_at
ESTs SEQ ID NO: 117 (DNA)	Consensus includes gb:AI300126 /FEA=EST /DB_XREF=gi:3959472 /DB_XREF=est:qn54f02.x1 /CLONE=IMAGE:1902075 /UG=Hs.257858 ESTs	240830_at
ESTs SEQ ID NO: 118 (DNA)	Consensus includes gb:AI917390 /FEA=EST /DB_XREF=gi:5637245 /DB_XREF=est:ts79a05.x1 /CLONE=IMAGE:2237456 /UG=Hs.99415 ESTs	240964_at
betacellulin SEQ ID NO: 119 (DNA)	Consensus includes gb:AI620677 /FEA=EST /DB_XREF=gi:4629803 /DB_XREF=est:tu85e09.x1 /CLONE=IMAGE:2257864 /UG=Hs.154191 ESTs	241412_at
ESTs	Consensus includes gb:H05025 /FEA=EST	241874_at

SEQ ID NO: 120 (DNA)	/DB_XREF=gi:868577 /DB_XREF=est:yl74g12.s1 /CLONE=IMAGE:43864 /UG=Hs.323767 ESTs	
ESTs SEQ ID NO: 121 (DNA)	Consensus includes gb:AW024656 /FEA=EST /DB_XREF=gi:5878186 /DB_XREF=est:wu78h05.x1 /CLONE=IMAGE:2526201 /UG=Hs.233382 ESTs, Moderately similar to AF119917 62 PRO2822 H.sapiens	242358_at
ESTs SEQ ID NO: 122 (DNA)	Consensus includes gb:BF696216 /FEA=EST /DB_XREF=gi:11981624 /DB_XREF=est:602124536F1 /CLONE=IMAGE:4281632 /UG=Hs.188724 ESTs	242626_at
ESTs SEQ ID NO: 123 (DNA)	Consensus includes gb:N57929 /FEA=EST /DB_XREF=gi:1201819 /DB_XREF=est:yv61e06.s1 /CLONE=IMAGE:247234 /UG=Hs.48100 ESTs	242978_x_at
ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY [H.sapiens] SEQ ID NO: 124 (DNA)	Consensus includes gb:AI457984 /FEA=EST /DB_XREF=gi:4312002 /DB_XREF=est:tj66a04.x1 /CLONE=IMAGE:2146446 /UG=Hs.165900 ESTs, Weakly similar to ALUC_HUMAN !!!! ALU CLASS C WARNING ENTRY !!! H.sapiens	243729_at
ESTs SEQ ID NO: 125 (DNA)	Consensus includes gb:AA581439 /FEA=EST /DB_XREF=gi:2359211 /DB_XREF=est:nh13c10.s1 /CLONE=IMAGE:952242 /UG=Hs.152328 ESTs	244650_at

Biological Validation of Biomarker Candidates: Modulation of Expression by
Treatment with Ligands for EGFR or by Treatment with Inhibitors for EGFR

To validate the significance of the biomarker candidates to predict the activity
5 of the EGFR pathway and thereby the sensitivity of cancer cell to inhibition of EGFR
by therapy, genes that would be regulated by the EGFR pathway were identified.
Demonstration of that property for the EGFR biomarker candidates described above
would add additional credibility as it would link these genes functionally to the EGFR
pathway. Colon cancer and a lung cancer cell lines were treated with epidermal

growth factor, in the absence of serum or, in the presence of serum with the EGFR modulator BMS-461453 or the EGFR modulator cetuximab (also known as C225, a chimeric monoclonal EGFR antibody). To identify genes induced by epidermal growth factor, serum starved cells were treated with 20ng/ml EGF for 0.5, 6, and 18
5 hours. Control cells were treated with media alone. The expression profiling was performed, and data was analyzed using GeneChip® Expression Analysis software MAS 5.0 (Affymetrix, Santa Clara, California).

Genes inhibited by EGFR antagonists were identified by treating cells in the presence of 10% serum with 0.5uM of BMS-461453 or 1ug/ml or 5ug/ml of C225 for
10 6 and 24 hours. Cells exposed to 0.05% DMSO were used as the experimental control. Expression profiling was performed, and data were analyzed using GeneChip® Expression Analysis software MAS 5.0.

The gene expression of the inhibitor or EGFR treated cell lines was compared pair-wise to the untreated controls. Polynucleotides from the biomarker list, in which
15 expression was increased two fold with EGFR exposure or decreased two fold with EGFR inhibitor treatment compared to the untreated controls, were considered to be modulated by EGFR. These biomarkers are provided in Table 4. Examples of the biomarkers include EphA1, B-cell translocation gene 2, prostaglandin-endoperoxide synthase 2 and serine (or cysteine) proteinase inhibitor (clade B), which are highly
20 expressed in sensitive cells and up regulated by treatment with EGFR. On the other hand, spondin 1, talin 2 and nuclear receptor subfamily 3 are genes whose expression levels correlate with sensitivity or resistance of colon cancer cell lines and are consistently down regulated by treatment with EGFR inhibitors BMS-461453 and C225. It appears that these biomarkers are likely to be directly or indirectly involved
25 in the EGFR signaling pathway, based on their expression modulation by EGF or EGFR inhibitor treatment.

Identification of Top Biomarkers

In an attempt to further prioritize biomarkers for use in predicting response of
30 cancer cells to treatment with one or more EGFR modulators, the following filter criteria were used on the Table 4 biomarkers to identify a total of fourteen biomarkers (Table 5) as the top biomarkers:

- (1) results from the highly significant correlation of gene expression with IC₅₀:
A p-value < 0.01 in the student TTEST or a Pearson value < - 0.6 described above;
- (2) results from the modulation of expression by EGFR ligand and/or EGFR inhibitor treatment described above; and
- 5 (3) biomarkers supported by literature revealing a direct relationship between the EGFR pathway and the biomarkers.

TABLE 5 - Top Fourteen Biomarkers

Biomarker Name	Literature Support Citation	Induced by EGF/ Inhibited by EGFR antagonist
mucin 2, intestinal/tracheal (MUC2)	J Biol Chem. 2002 Aug 30;277(35):32258-67	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
intestinal mucin 3 (MUC3)	No	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
Homo sapiens cystic fibrosis transmembrane conductance regulator ATP-binding cassette (sub-family C, member 7) (CFTR)	No	Expression stimulated 2 fold by EGFR in H292 lung cancer cell line
f-spondin (KIAA0762) protein	No	Expression inhibited 2 fold by EGFR antagonist in LOVO colon cancer cell line
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	J Invest Dermatol. 2000 Jan;114(1):83-7	Expression stimulated 3 fold by EGFR in H292 lung cancer cell line
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5)	Electrophoresis. 2001 Aug;22(14):3001-8.	Expression stimulated 2 fold by EGFR in H292 lung cancer cell line
BTG family, member 2 (BTG2)	No	Expression stimulated 2 fold by EGFR in H292 lung cancer cell line
talin 2 (TLN2)	No	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
arachidonic acid	J Biol Chem. 1994 Aug	no

epoxygenase	26;269(34):21786-92.	
prostaglandin G/H synthase and cyclooxygenase	J Biol Chem. 1994 Aug 26;269(34):21786-92.	Expression stimulated 6 fold by EGFR in H292 lung cancer cell line
EphA1 (EPHA1)	No	Expression stimulated 2 fold by EGFR in CACO2 colon cancer cell line
hemoglobin, alpha 1 (HBA1)	No	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
bone morphogenetic protein 2	Development 2000 Nov;127(22):4993-5005	no
betacellulin (BTC)*	Biochem Biophys Res Commun. 2002 Jun 28;294(5):1040-6	no

*The gene betacellulin showed counter regulation with EGFR expression as defined for the EGFR-A list but had just a p value of 0.04 in the Student's TTest for correlation with IC₅₀. It was still selected as a top biomarker for the strong literature support, as betacellulin is one of the published ligands of EGFR.

5

Utility of Biomarkers

Polynucleotides that correlate to a specific property of a biological system can be used to make predictions about that biological system and other biological systems. To show the predictive utility of biomarkers that correlate to EGFR modulator sensitivity and resistance, these polynucleotides were tested for their ability to predict the response of twenty two colon cancer cell lines to a small molecule EGFR modulator.

10

The invention includes single biomarkers including, for example, the fourteen top biomarkers which were tested in a voting scheme. For that purpose, the mean expression value was calculated for all fourteen biomarkers. Colon cancer cell lines which showed an expression level above the mean were then voted to be sensitive, and colon cancer cell lines with expression levels below the mean were voted to be resistant. After this procedure, the voting was compared to the actual sensitivity/resistance status according to the definition based on IC₅₀ (see above) and an error rate was calculated. The error rates of the fourteen top biomarkers are shown in Table 6.

15

20

TABLE 6 - Error Rates of Fourteen Top Biomarkers

Biomarker Name	Pearsons value	TTEST P value	Prediction error rate
mucin 2,	-0.531	0.0083	20%

intestinal/tracheal (MUC2)			
intestinal mucin 3 (MUC3)	-0.639	0.0004	11.72%
Homo sapiens cystic fibrosis transmembrane conductance regulator ATP-binding cassette (sub-family C, member 7) (CFTR)	-0.646	9E-05	5.9%
f-spondin (KIAA0762) protein	-0.622	0.0004	12.8%
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	-0.575	0.0029	21.75%
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5)	-0.62	0.0028	21.75%
BTG family, member 2 (BTG2)	-0.544	0.0042	20.5%
taln 2 (TLN2)	-0.874	3E-05	8.8%
EphA1 (EPHA1)	-0.647	0.0021	22%
hemoglobin, alpha 1 (HBA1)	-0.744	8E-05	20%
bone morphogenetic protein 2	-0.555	0.0091	31.8%
betacellulin (BTC)	-0.536	0.047	43.5%

The biomarkers talin, the Cystic fibrosis conductance regulator (CFTR), and mucin 3 were the best single biomarkers with error rates below 12%.

5

EXAMPLES:

EXAMPLE 1 - METHODS

IC₅₀ determination--*in vitro* cytotoxicity assay

A small molecule EGFR inhibitor, erlotinib HCl (BMS-461453), was tested for cytotoxicity *in vitro* against a panel of twenty-two human colon cancer cell lines

available from the American Type Culture Collection. Cytotoxicity was assessed in cells by MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulphenyl)-2H-tetrazolium, inner salt) assay (T.L. Riss et al., 1992, *Mol. Biol. Cell*, 3 (Suppl.):184a).

5 To carry out the assays, the colon cells were plated at 4,000 cell/well in 96 well microtiter plates and 24 hours later serial diluted drugs were added. The concentration range for the EGFR inhibitor was from 5 $\mu\text{g/ml}$ to 0.0016 $\mu\text{g/ml}$ (roughly 10 μM to 0.0032 μM). The cells were incubated at 37 °C for 72 hours at which time the tetrazolium dye MTS (333 $\mu\text{g/ml}$ final concentration) in combination
10 with the electron coupling agent phenazine methosulfate (25 μM final concentration) was added. A dehydrogenase enzyme in live cells reduces the MTS to a form that absorbs light at 492 nm that can be quantified spectrophotometrically. The greater the absorbency, the greater the number of live cells. The results were expressed as an IC_{50} , which is the drug concentration required to inhibit cell proliferation (i.e.,
15 absorbance at 450 nm) to 50% of that of untreated control cells. The mean IC_{50} and standard deviation (SD) from multiple tests for each cell line were calculated.

Resistant/sensitive classification

The cell lines with IC_{50} below 6 μM were defined as sensitive to the EGFR
20 inhibitor, whereas those with IC_{50} above 6 μM were considered to be resistant. The resistant/sensitive classification are shown above in Table 1, with five cell lines classified as sensitive and seventeen cell lines classified as resistant.

Gene expression profiling

25 The colon cells were grown using standard cell culture conditions: RPMI 1640 supplemented to contain 10% fetal bovine serum, 100 IU/ml penicillin, 100 mg/ml streptomycin, 2 mM L-glutamine and 10 mM Hepes (all from GibcoBRL, Rockville, Maryland). RNA was isolated from 50-70% confluent cells or drug-treated cells using the RNeasy™ kits commercially available from Qiagen (Valencia,
30 California). Quality of the RNA was checked by measuring the 28s:18s ribosomal RNA ratio using Agilent 2100 bioanalyzer (Agilent, Technologies, Rockville, Maryland). Concentration of total RNA was determined spectrophotometrically. 10

5 μ g of total RNA from each cell line was used to prepare biotinylated probe according to the Affymetrix Genechip® Expression Analysis Technical Manual, 2001. Targets were hybridized to Affymetrix high density oligonucleotide array human HG-U133 set chips (Affymetrix, Santa Clara, California). Arrays were then washed, and stained using the GeneChip Fluidics station according to the manufacture's instructions. The HG-U133 set consisting of two GeneChip® arrays contains nearly 45,000 probe sets representing more than 39,000 transcripts derived from approximately 33,000 well-substantiated human genes.

10 Preprocessing of microarray data for selecting biomarkers

Scanned image files were visually inspected for artifacts and analyzed with GeneChip® Expression Analysis software MAS 5.0 (Affymetrix, Santa Clara, California). The "Detection Call" (see Affymetrix manual) was used to determine whether a transcript was detected within one sample, as well as the "Signal" (see Affymetrix Genechip® Expression Analysis Technical Manual, 2001) which measured the relative abundance of a transcript. The trimmed mean intensity for each chip was scaled to 1,500 (see Affymetrix manual) in order to account for any minor differences in global chip intensity, so that the overall expression level for each cell line is comparable. Affymetrix control sequences were removed prior to analysis.

20

Induction Studies of colon and breast cell lines with EGFR inhibitors or EGFR ligand and selection of genes modulated by the inductions

The five colon cell lines and one lung cell line indicated with asterisks in Table 1 were used in the drug induction study. Three of the colon cell lines express EGFR and are sensitive to the EGFR inhibitor BMS-461453. The SW480 cell line, while expressing EGFR, is insensitive to the EGFR inhibitor, and the COLO320_DM does not express EGFR and is EGFR inhibitor resistant. The lung cancer cell line H292 expresses EGFR, but its sensitivity status is unknown. Cells were seeded in a 10 cm² culture plate with the medium described above and cultured for 24 hours.

30 For the EGF induction studies, the colon cell line CACO2 and the lung cancer H292 cell line were washed 2X PBS, and the media was changed to RPMI without serum. The next day the cells were treated with 20 ng/ml EGF, and eventually lysed

for RNA isolation 0.5, 6 and 18 hours post treatment. Gene expression was profiled as described below.

EGFR inhibition studies were conducted on the colon cell lines GEO, CCD33-CO, SW480 and COLO320DM. The expression profiling was performed as described above and data was analyzed using GeneChip® Expression Analysis software MAS 5.0. The expression data of EGFR inhibitor treated cell lines were compared pair-wise to that of untreated same cell line. A change was considered significant if a two fold difference in expression was demonstrated between the treated and the untreated control. Analysis was done for all four cell lines to compare the gene expression with or without EGFR inhibitor treatment.

EXAMPLE 2 - RT-PCR EXPRESSION PROFILING

RNA quantification was performed using the SYBR Green real-time PCR. The SYBR Green real-time PCR assay is one of the most precise methods for assaying the concentration of nucleic acid templates.

RNA can be prepared using standard methods, preferably, employing the RNeasy Kit commercially available from Qiagen (Valencia, California). cDNA template for real-time PCR can be generated using the Superscript™ First Strand Synthesis system for RT-PCR. SYBR Green real-time PCR reactions are prepared as follows: the reaction mix contains 20 ng first strand cDNA; 50 nM Forward Primer; 50 nM Reverse Primer; 0.75X SYBR Green I (Sigma); 1X SYBR Green PCR Buffer (50mM Tris-HCl pH 8.3, 75 mM KCl); 10% DMSO; 3 mM MgCl₂; 300 μM each dATP, dGTP, dTTP, dCTP; 1 U Platinum® Taq DNA Polymerase High Fidelity (Cat# 11304-029; Life Technologies; Rockville, Maryland). Real-time PCR is performed using an Applied Biosystems 5700 Sequence Detection System.

Conditions are 95 °C for 10 minutes (denaturation and activation of Platinum® Taq DNA Polymerase), 40 cycles of PCR (95 °C for 15 seconds, 60 °C for 1 minute). PCR products are analyzed for uniform melting using an analysis algorithm built into the 5700 Sequence Detection System.

cDNA quantification used in the normalization of template quantity is performed using SYBR Green real-time PCR. Expression of EGFR is normalized to GAPDH expression as described below.

The sequences for the GAPDH oligonucleotides used in the SYBR Green real-time PCR reactions are:

GAPDH-F: 5'-AGCCGAGCCACATCGCT-3' (SEQ ID NO: 191)

GAPDH-R: 5'-GTGACCAGGCGCCCAATAC-3' (SEQ ID NO: 192)

5 The sequences for the EGFR oligonucleotides used in the SYBR Green real-time PCR reactions are:

EGFR-F: 5'- GCGTCTCTTGCCGGAATGT-3' (SEQ ID NO: 193)

EGFR-R: 5'- AGCCGAGGCAGGGAATGCGTG-3' (SEQ ID NO: 194)

The Sequence Detection System generates a Ct (threshold cycle) value that is
 10 used to calculate a concentration for each input cDNA template. cDNA levels for each gene of interest are normalized to GAPDH cDNA levels to compensate for variations in total cDNA quantity in the input sample. This is done by generating GAPDH Ct values for each cell line. Ct values for the gene of interest and GAPDH are inserted into a modified version of the $\delta\delta C_t$ equation (Applied Biosystems
 15 Prism® 5700 Sequence Detection System User Manual) which is used to calculate a GAPDH normalized relative cDNA level for each specific cDNA. The $\delta\delta C_t$ equation is: relative quantity of nucleic acid template = $2^{\delta\delta C_t} = 2^{(\delta C_{ta} - \delta C_{tb})}$, where $\delta C_{ta} = C_t$ target – Ct GAPDH, and $\delta C_{tb} = C_t$ reference – Ct GAPDH.

20 EXAMPLE 3 - PRODUCTION OF ANTIBODIES AGAINST THE BIOMARKERS

Antibodies against the biomarkers can be prepared by a variety of methods. For example, cells expressing an biomarker polypeptide can be administered to an animal to induce the production of sera containing polyclonal antibodies directed to the expressed polypeptides. In one aspect, the biomarker protein is prepared and
 25 isolated or otherwise purified to render it substantially free of natural contaminants, using techniques commonly practiced in the art. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity for the expressed and isolated polypeptide.

In one aspect, the antibodies of the invention are monoclonal antibodies (or
 30 protein binding fragments thereof). Cells expressing the biomarker polypeptide can be cultured in any suitable tissue culture medium, however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented to contain 10% fetal bovine

serum (inactivated at about 56 °C), and supplemented to contain about 10 g/l nonessential amino acids, about 1,00 U/ml penicillin, and about 100 µg/ml streptomycin.

5 The splenocytes of immunized (and boosted) mice can be extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line can be employed in accordance with the invention, however, it is preferable to employ the parent myeloma cell line (SP2/0), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (1981, *Gastroenterology*, 80:225-232).
10 The hybridoma cells obtained through such a selection are then assayed to identify those cell clones that secrete antibodies capable of binding to the polypeptide immunogen, or a portion thereof.

Alternatively, additional antibodies capable of binding to the biomarker polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies.
15 Such a method makes use of the fact that antibodies are themselves antigens and, therefore, it is possible to obtain an antibody that binds to a second antibody. In accordance with this method, protein specific antibodies can be used to immunize an animal, preferably a mouse. The splenocytes of such an immunized animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify
20 clones that produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce the formation of further protein-specific antibodies.

25 EXAMPLE 4 - IMMUNOFLUORESCENCE ASSAYS

The following immunofluorescence protocol may be used, for example, to verify EGFR biomarker protein expression on cells or, for example, to check for the presence of one or more antibodies that bind EGFR biomarkers expressed on the surface of cells. Briefly, Lab-Tek II chamber slides are coated overnight at 4 °C with
30 10 micrograms/milliliter (µg/ml) of bovine collagen Type II in DPBS containing calcium and magnesium (DPBS++). The slides are then washed twice with cold DPBS++ and seeded with 8000 CHO-CCR5 or CHO pC4 transfected cells in a total

volume of 125 μ l and incubated at 37 °C in the presence of 95% oxygen / 5% carbon dioxide.

The culture medium is gently removed by aspiration and the adherent cells are washed twice with DPBS++ at ambient temperature. The slides are blocked with
5 DPBS++ containing 0.2% BSA (blocker) at 0-4 °C for one hour. The blocking solution is gently removed by aspiration, and 125 μ l of antibody containing solution (an antibody containing solution may be, for example, a hybridoma culture supernatant which is usually used undiluted, or serum/plasma which is usually diluted, e.g., a dilution of about 1/100 dilution). The slides are incubated for 1 hour at
10 0-4 °C. Antibody solutions are then gently removed by aspiration and the cells are washed five times with 400 μ l of ice cold blocking solution. Next, 125 μ l of 1 μ g/ml rhodamine labeled secondary antibody (e.g., anti-human IgG) in blocker solution is added to the cells. Again, cells are incubated for 1 hour at 0-4 °C.

The secondary antibody solution is then gently removed by aspiration and the
15 cells are washed three times with 400 μ l of ice cold blocking solution, and five times with cold DPBS++. The cells are then fixed with 125 μ l of 3.7% formaldehyde in DPBS++ for 15 minutes at ambient temperature. Thereafter, the cells are washed five times with 400 μ l of DPBS++ at ambient temperature. Finally, the cells are mounted
20 in 50% aqueous glycerol and viewed in a fluorescence microscope using rhodamine filters.

CLAIMS:

What is claimed is:

1. A method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises:
 - (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4;
 - (b) exposing the mammal to the EGFR modulator;
 - (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker,wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.
2. The method of claim 1 wherein the at least one biomarker is selected from the biomarkers of Table 5.
3. The method of claim 1 wherein the method is an in vitro method, and wherein the at least one biomarker is measured in at least one mammalian biological sample from the mammal.
4. A method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises:
 - (a) exposing the mammal to the EGFR modulator;
 - (b) following the exposing of step (a), measuring in the mammal the level of the at least one biomarker selected from the biomarkers of Table 4,wherein a difference in the level of the at least one biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said EGFR modulator, indicates that the mammal will respond therapeutically to said method of treating cancer.

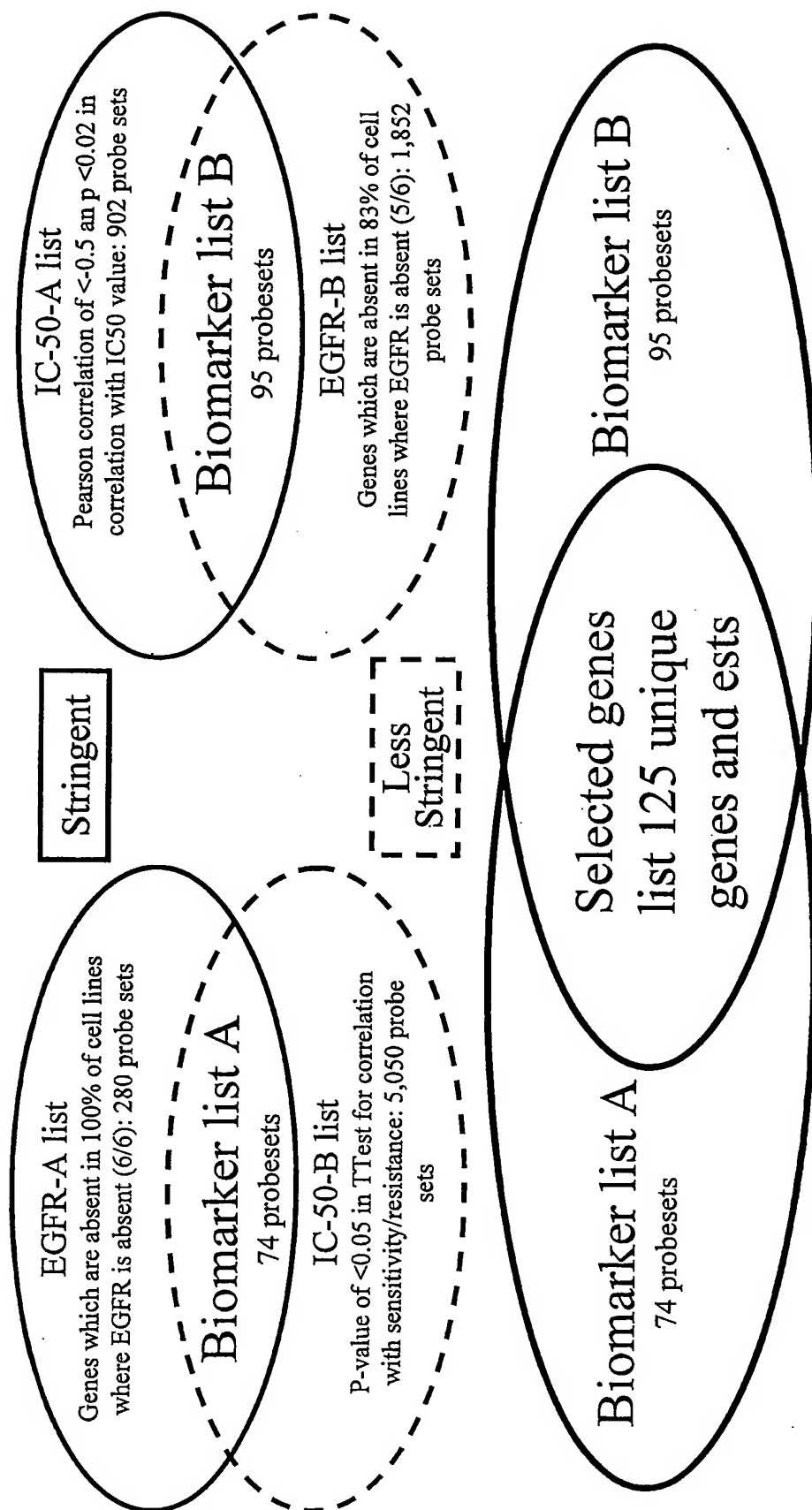


FIG. 1

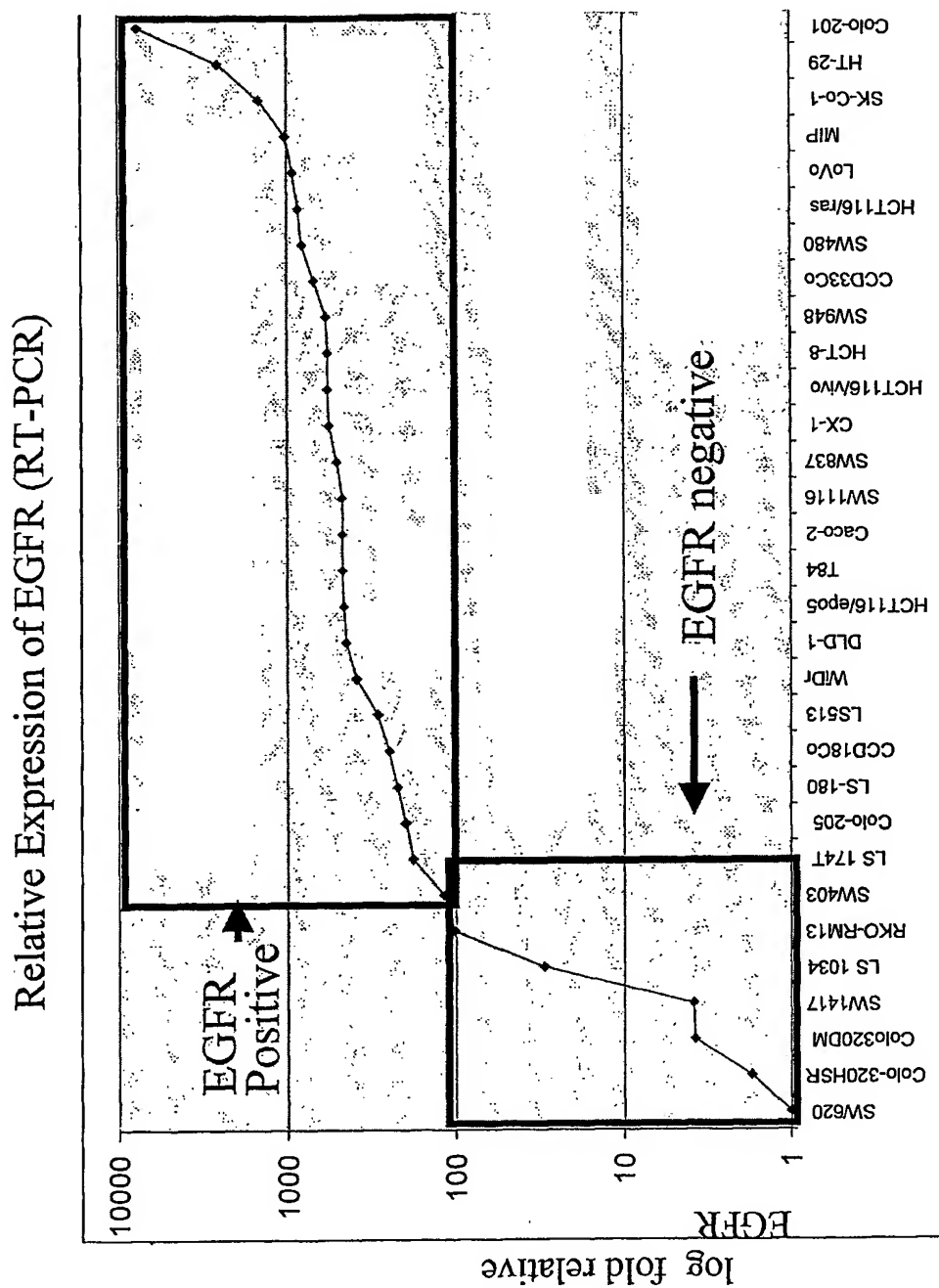


FIG. 2A

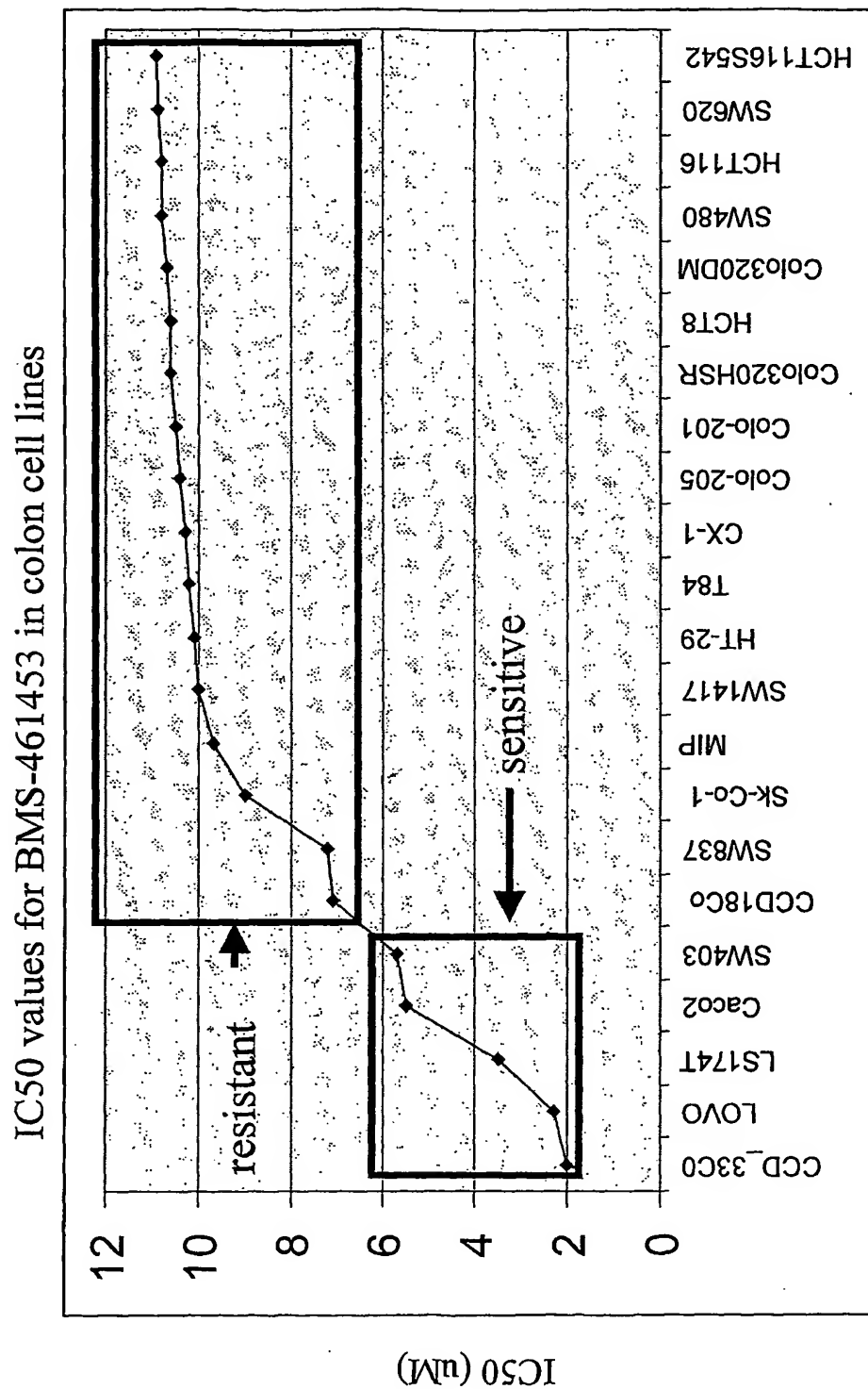


FIG. 2B

SEQUENCE LISTING

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<211> 701
<212> DNA
<213> Human

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2800

<210> 69

<211> 1634

<212> DNA

<213> Human

<400> 69

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taactcctcc acataagcgg caggaaaatg gccctttttc ccattcaaag atccaaacca	180
ccatccttct tcttttttct cgtgtataat cacaatgtca cccttttcca aattcaactc	240
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aagaacagat gtgacctgtt tgcagaaatt ctctccattt tgagaaaact ccttttaggtt 1560
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<210> 70
<211> 774
<212> DNA
<213> Human

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<222> (465)..(465)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (509)..(509)
<223> n is a, c, g, or t

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<221> misc_feature
<222> (617)..(617)
<223> n is a, c, g, or t

<220>
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<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (667)..(667)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (693)..(693)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (740)..(740)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (762)..(762)
<223> n is a, c, g, or t

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atattaactc tctaaaaaat actcagaata gatctgtaat cttcctcctc ctcctccgaa 120

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ctggagccaa tcttcttctt taaacgctga tggattgcat acatgtatgt cttccatata 180
agccacatac acaacattca gatacacttc cctctgtgca gggggataca ccagcctcct 240
gccaggttct ggaagctcac cttataatct accaggataa agctgtgtgc tgagtaggag 300
gttatggtgg ggttggggag taacaaggag ataaaagacc ttgtggtccc aacttcctta 360
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gctaactgaa ggccaagctc ccagagaagc tggactcact gtgtnggatt actgagggtg 480
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ttaagancca gacaccagtc ttcagagagc ctncgaggt agccgcaaca ttctgcagc 720
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<210> 71
<211> 578
<212> DNA
<213> Human

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<400> 71
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agggtaatgg aaagaatata atctcgtaat ttataactta aggctgtaaa tggcaaagtc 180
ccatagatat ttaaaaaatct atatttgtat ttatttataa tatagatata ggccctcaag 240
gattcataga gatttatgta ataaactaga ttttggact atttattttg ttgttgttgt 300
tgcttgtag gtaagcaaac ccaaacaat taagtcctga aaagtgggat gaaatccaa 360
aggaactcta tgagaccaca cagaactctt ttaataaata tggcccatc aaattccata 420
tccagtgaat atcattttga tccacaatca tgttgatgtt tctatggagg atacttctag 480
cagctgtgat ttcttttgta gcattctggc tctccaactc tattcatata attgagtatg 540
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<210> 72
<211> 475
<212> DNA
<213> Human

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<223> n is a, c, g, or t

<220>

<221> misc_feature

<222> (361)..(361)

<223> n is a, c, g, or t

<400> 72

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ttttgccct cctggatgtg aacggaatct cccctcctca cctccacaga gggagctcaa      180
gccccaggga accttcccct ccccttttat gcattaccag gggagtggca ggggcagccc      240
ccaactgtgg agtgcattca ggtctgaggg gggaggaagg ctcanagggg catctcccca      300
gcacctgcc acagtgtctg cttctggggg gtttgttcag cggcctgtg ggctgcccc      360
ngctgggggc tccccagct ccccgatcat cctggcttgt tccacggagc cctgagccaa      420
gtctttgtct ggctcatgtt cctctcaca catcccacag gcaggggtga gcctg      475

```

<210> 73

<211> 512

<212> DNA

<213> Human

<400> 73

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catgtaaaac tgacttttat tacaattaaa aaagaacaaa gacaatttga taagtgcctt      60
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tttattacat gtaaactata agatattaca agttaaaactc cagtcttttc tggatattca      180
attgaaatac tactggcaga aacatacaga aaacaaatac ccatttcagt tcctcaggta      240
ccattactgg ttgaatgatc aagatctggc cacagaagag aagtggaaat atgcatcaaa      300
acaaaactta ttcttaacat gactaacagt attgttattt aaaccctaaa cataattaat      360
aattggatca ttaaaaacac atcttcaatt tatatagcac ctttcttccg aagagttgaa      420
agcattcgtg cttatctcta ttatttcgtt tgtccccata acatctctat gaggtaggca      480
atgggttagta tcattatccc cattttgtat at      512

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<210> 74

<211> 668

<212> DNA

<213> Human

<400> 74

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tttcaaaacc agcaaaaatt aaatttaatt gggctcaagt ctgggcagtt tgccttct      60
caggaccagc cgtcagcagt ccctgacgaa agcaccocat tctctccaca gacagctggt      120

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tccaaaagga ccctctgagg ctggtcttcc gggtaggatg tgctgtggga gggttctgtt 180
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ggaaatatct tatggaattt cactaggtgc ataacttctc ctaagtgcac gtcaaagcc 660
tgctggcg 668

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<210> 75
<211> 568
<212> DNA
<213> Human

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<400> 75
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aatgcacacc aaattattct gtttttagga aaagcagtag gattggtcag ggcatggaat 180
gtcggctaag tgaagtgaga tttaaaattt ttattctaca tgattttcta gtgttgggaa 240
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gtacctagaa atgattttgg atctcttcac agagaccctt atcccaccaa cctccaatcc 480
tcccaccata cattgatccc tttctatctg cttggatcat tagctgtaaa ttttaactcg 540
aaaaacaag tacgtttaat cattgtac 568

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<210> 76
<211> 491
<212> DNA
<213> Human

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<220>
<221> misc_feature
<222> (371)..(371)
<223> n is a, c, g, or t

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<220>
 <221> misc_feature
 <222> (394)..(394)
 <223> n is a, c, g, or t

 <400> 76
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 aaccaagccg gcgttttctt gtcaccatgc cgtattcgcc tccccgtact atcaaatgt 480
 acttatccaa t 491

<210> 77
 <211> 2437
 <212> DNA
 <213> Human

<400> 77
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 atgaggtcct gcctgtggag atgcaggcac ctgagccaag gcggtccagtg gtccttgctt 120
 ctggctgtcc tggctcttctt tctcttcgcc ttgccctctt ttattaagga gcctcaaaca 180
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 ggaaaggagg ccaaccaggc accgccggag gagcaggaca aggtgcccc caacagcacag 420
 agggcagcat ggaagagccc agaaaaagag aaaacatgg tgaacacact gtcaccaga 480
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<210> 78
 <211> 582
 <212> DNA

<213> Human

<400> 78
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 ttcttcatga aatttgactt ctttgaagtg aaggcttttt tctatcatct cttatagctc 180
 tgactgaata agtcttaatg ctttcttcat gttttctatc aataggggta aatcccagg 240
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 agggctctaca aacatgattc taggcacata ttgccatca ggtgataaat tcttatcagt 360
 ggtttcatgc ataaggttta gcatgatgaa cttattctga gccatttctt gtatttcttc 420
 attttgggca aatactttct ttagtgcttg agagtattga caatcctcca ggtgatgaat 480
 aaccattaat ggcttcttac ttttttgagc ataaaagaga ccttgctcat aagtttgtag 540
 ccaagagatg gcatctaccc atcctcttga gagtgactga gg 582

<210> 79

<211> 511

<212> DNA

<213> Human

<400> 79
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 gcatgcatta catggttcat aatgctattc caattaggct tttcatagtg ccttctcata 120
 acgtccttta aaaaaataa taactgaaag ggaaaagaaa gtgtcaattg caattacatt 180
 taaaaacca aactgctgct ttcaattaga gtgaatctgt gcttcgctac tcagatatac 240
 acatgtagat tttccaaggc ccatgcacac acttctgtag gggcagaaat tttctatgaa 300
 taatggcttt agcaaccga atagtatctc taaacattga caagcttggg gaacagggca 360
 acaagtgcaa tgaacaatac aatttctaac gtttgtcca gtcaacatac cactttgccc 420
 tggagatatt taacacagca tttcattttt ggaatgataa gggataattc atctaattaa 480
 gggattata cagaatatac ctataaaaga c 511

<210> 80

<211> 987

<212> DNA

<213> Human

<400> 80
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ttgatagtga tagactataa tccatattta aattttatag agaagaaatt ttattgtact	180
gtgatgtaga tatttattat ccaggtaagg atttgcccgg tgtgtatttt ttacaattga	240
gacattttac tttaatcttt aacaaaaaat gcattaaaaa cactcaca aaaaaacaaa	300
aaaaaaaaaa aaagacaacc caaacggggg gggaaaaaag aggtgattgg caccctttat	360
cacgaaaatc ttctgcggg cgccctcta ataaccagtc ttctggaaca actgtgcca	420
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gaattccata tattaatgaa tgtgagatta agtatagagt gaagacatta acacacaatt	180
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<213> Human

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cacaaaataa gctcttaatg caagaaatga atctccagga tagatcatac taatctatcc      180
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aactaagcct ctttggggca ggagactttg gaagtgttga aggagagtag aatctattca      480
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<211> 505

<212> DNA

<213> Human

<400> 83

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<212> DNA

<213> Human

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<400> 89
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 <212> DNA
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<210> 97
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 <213> Human

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 <223> n is a, c, g, or t

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 <223> n is a, c, g, or t

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 <223> n is a, c, g, or t

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 gcctaccctt aaaagccaaa 140

<210> 98

<211> 492
 <212> DNA
 <213> Human

<400> 98
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 cactaggaga ttactaaaac tgtagggcac attcatcttc ctacaattct tcaccacaaa 180
 aataaaatcc aatttaggag gctccattaa ctcttttaaat atatttctaa atcttaaate 240
 tatatttcaa aatgaacatg gtacttcata tggggccact tttcataatt ctttcaactc 300
 aatgttttag ccaaaactgc aaacatttga aatttaattt tgaataaaaa ttacagctta 360
 tgcaccaaga taacattaga aagtgtcttc agacatttta tcagggtattt tcctcattac 420
 acccaaccaa acacagaaag aaatatatat ttttgaaatg tcaattactg ctatgctatc 480
 aaaagctgac at 492

<210> 99
 <211> 275
 <212> DNA
 <213> Human

<400> 99
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 ctgcttttat ctgaaagagg ggggaccact gttgtctcag tcacaaaaat tctgctgagt 180
 gtctttccac tggaaatacc ataagataag ctctcataag acaatttcac tattccaagg 240
 gcagaatgtg gcaaaaagtg ggctgctgct agctt 275

<210> 100
 <211> 222
 <212> DNA
 <213> Human

<400> 100
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 ggtattcggg catgagagca gcaggggcct cctgacgcgg gcaggagaaa catggcaccc 180
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<210> 101
 <211> 440
 <212> DNA

<213> Human

<400> 101

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cttaaaatg acatagtaaa aaagacctag atgtgatagt aaacccttat tttttaatat    180
accaaacagt tgtaaccaca aaagcactgt aatcatcatt tcttgaaaaa gttataagca    240
tatttgaaac ttgaaacttc taaaatcttg gttagagaag aaaactaaat tctacattta    300
gtggaattaa gcttctacct aatagctttt ataccaactt tccaaaagta ggagtgggtac    360
caggtttcca tgtaaaccca agaaagcagt ttatccatcc acacagccca acccttgctc    420
caatgagcat attactgggt                                     440
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<210> 102

<211> 559

<212> DNA

<213> Human

<220>

<221> misc_feature

<222> (548)..(548)

<223> n is a, c, g, or t

<400> 102

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gagtctcact ctgtcgcca ggctggagtg cagtggccag atctcagctc actgaaacct    180
cagcctccca agttcaagtg attctcgtac ctgagcctcc tgagtagctg gaattccagg    240
ctgtactcac tgctttgctc atatccccgc tcattaccag ggacaggcca gcacccttg    300
cattgcatct cacatatcca ctgatggatg gagaacagac tgaaattcag tgccttagag    360
accacacact ccaaccccct cattgtgcag atgggaaaac tgagagccat agaagggaag    420
tggtttgccc aaagccacac ttactgtttt cccacactg taccacaaac tttcaccatt    480
cttcaggttt ggaaaaatac taataaactg atcaacacta aaaaaaaaaa agcggccgct    540
cggttgtngc gcggccggg                                     559
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<210> 103

<211> 388

<212> DNA

<213> Human

<400> 103

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 atttatatgg cttcattttc ttacatttgg atcctggatc cagatggagt tcattcttgc 180
 atatggtgtg aagtacaggt ctaacttcaa ctttctcaa ggggctttcc agttggctca 240
 gcaccattta ttaaagtctg ctttgacctg cgattgaaga tgccaccttt aactcctcat 300
 cccccacccc taagaaacct cacggaacat atgacccaag agcagagcag acataaaaag 360
 attaactgag ctactgagat tcggtcaa 388

<210> 104
 <211> 545
 <212> DNA
 <213> Human

<400> 104
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 ctgtcattta tgggcattta atttctttga ataaatttaa caagttgcaa atgaatatatt 120
 agcaaattgc actcagatta aaataacaaa ataattctctt atcagaagct aagaaatata 180
 ttttcctcct cctcatccat atccaaagac ggttctgaaa atgccttttc ttctctatta 240
 tagcaacacc tagtggcttg agaaggccag gtctagaggt atgcatttac ggctgggaaa 300
 cactgacctt tagctttgaa gacctcaggt agcacctaga cgtcggctat aaccgcataa 360
 caatggtccc catctgaaac catttaagtc agaattcttg gaggaagagg ccaggattgg 420
 taggttataa aagttgcccga gatgatttta atgtgcagcc aaggctaaga gctacttata 480
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 ctggg 545

<210> 105
 <211> 580
 <212> DNA
 <213> Human

<400> 105
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 ggctgataga gaatcatgtg taactggggt cagcattcct ataatttttt gagccaaaga 180
 cagaatacac actttaccct gacaggtttc ttccagaatt taggacagct gatgaaatga 240
 aaagacacac acccaagcca agagtgcaaa aggatgtagt agcatgattc cgccaaccaa 300
 atgcctcata ccctcagacg tcccaaattc agtggtgagc aggtaaattt ttaacaacaa 360

tctttctttg tgaggaaaaa agttcctgat ttccataatg taaatacttt cactgactgg 420
 tttgaagcca tcaacacgtc aactaacaat tgggttcctgc atgtctataa gctggcttta 480
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<210> 106
 <211> 618
 <212> DNA
 <213> Human

<400> 106
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 ttggatgtag cagctccaaa tagaggttac ctgattattg cttttataat tgaattctta 180
 aagagtttac atcataatta tataattgta tttttaaaca tcacagaaac ccaacatgta 240
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 tgtgctatta gtggccattg caagaaggaa gatgctgttt tcaataacag gaaatcaaga 420
 acaaacaaaa taatcgtctt ccatttaaaa aaaaaagaaa gcctacagaa aagtgaaaag 480
 gacaggggcc taaaaacatc tagtgatgcc aataaaatgg aatgtttttt aaaaagtgat 540
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 aacagacgct tttggtgc 618

<210> 107
 <211> 538
 <212> DNA
 <213> Human

<400> 107
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 aaagttttcc ttggcttttg gttatgggct gtctgctgaa tatgagtctt ggatcttttt 180
 cagcatcaac ttgcaaaagc tatgcctttc cacccttgcc ctgttagctt ttttgagtcc 240
 aggtctcccc actcccatgc caatggaccc tttataatgg ggaaggcatc acagcaagac 300
 gcaggcttgg ggctttccca atgaccaggt tctcattaag tgccatctca ccatcaacca 360
 gcgacagcaa tgtccctttt gcccaagctc ctcttttccc tgcactctgg ttgccctcta 420

aatggcacca gcccaaacca gggacagtca ctctgccact cacttcccaa atatttacag 480
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<210> 108
 <211> 542
 <212> DNA
 <213> Human

<400> 108
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 aattaatttc tggccacaaa ttctattttt acagcatgta attgaaacca gattaccttt 180
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 ggtgttccaa aaatatatac tatacagcaa ttctaaagt tataaatgtc ttggcgcat 480
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 ca 542

<210> 109
 <211> 484
 <212> DNA
 <213> Human

<400> 109
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 catgtagttt tcttctttct ctgtgttcta ttttattatt gtaaccactt tggcttttt 180
 tttgtataa tcaattgcag ctagaatggg gtatggctct taatagatat ttggataat 240
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 tctgttttaa tcagtaagtg attttaactt tcttcattat cccctcctct tgtttaactg 360
 tggataagta gttcccatgg attgcttcct ctgtcttctt agcgagaa atcggtggct 420
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 ttca 484

<210> 110
 <211> 478

<212> DNA
<213> Human

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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 <223> n is a, c, g, or t

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 <222> (439)..(439)
 <223> n is a, c, g, or t

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 <223> n is a, c, g, or t

<220>
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 <223> n is a, c, g, or t

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 aaaacaaatg gagtgggnca caggaattnt cagaaatgga ggcttaggct gtccatacag 120
 gattcagcaa gtacttgggg actgcgacta gaagaagcca gggtnggan taagtagctg 180
 aggaggagag ggagctgatn tggaggagag caagggcaac ttcaaggaac aaaagggaag 240
 ctgcaagnac cagctccatt aattcagcan acattccttg tctgtatgcc atgccagggt 300
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 cagangccaa agcaaagant tcctnaaagg tagccggcct gntgcaaac ctggggacaa 420
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<210> 111
 <211> 313
 <212> DNA
 <213> Human

<400> 111
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 ggcccgcgcc gccgaccccc tacaaaagcc ctctgcccac cccccaccac cgggcgtgcc 180
 tcgagccgcc ggccggcggt acaacaatat atatttatat ataatatata taaaacacag 240
 agtcaggaaa ggccgggtaga aatatgaaat ccgtataaat gtgttgtttc cttcattaaa 300

gtgtcttcgg gga 313

<210> 112
<211> 498
<212> DNA
<213> Human

<400> 112
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cttaggtttt tactgctccc attcttgctt ttactaattt atccaagatt agatgtgatt 180
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caggcttgga ggcttgagat atgtacgtga tagcctcct cccagtcac acaactggta 420
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<210> 113
<211> 590
<212> DNA
<213> Human

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<221> misc_feature
<222> (450)..(450)
<223> n is a, c, g, or t

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<222> (515)..(515)
<223> n is a, c, g, or t

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<221> misc_feature
<222> (547)..(547)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (558)..(558)
<223> n is a, c, g, or t

<220>
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<222> (570)..(570)
<223> n is a, c, g, or t

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<222> (581)..(581)

<223> n is a, c, g, or t

<400> 113

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aatgatgtac atttatgaac gacgactaga agtgaacatg aataactgaa aacaaacagt	180
gtgatgcaag tgaatttttg gagggtgaga tggtcattat attgtttctc gagcaattaa	240
atatttttatt ttcttcccaa aacaatgtcc acaagggggc agacagaaga tgacaaataa	300
aaccatttaa taaaaacctc agctgaaaag ctaataactc cagaatgcag gttgaaagca	360
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cgccactgca caccagcctg tgccacaaag taganttcgt ccaaaaaaaaa aaaaatcctc	540
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<210> 114

<211> 365

<212> DNA

<213> Human

<400> 114

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tccataagtc ataatttaac gtgcagtaag aacccatgaa gttgtctgac caaaagtaac	180
actcttctgt tgggaaagat ttacatcct tttattctgg atgaatcctg aattctagat	240
gttgggttta atgcttcaca caatggcaca ttacaagag gtacaaaaca cttattgagc	300
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gattc	365

<210> 115

<211> 539

<212> DNA

<213> Human

<220>

<221> misc_feature

<222> (359)..(359)

<223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (481)..(481)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (483)..(483)
 <223> n is a, c, g, or t

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 tctctactaa actgcagctc agttctgcct ctcataatat gtatgttgag taacattatg 180
 accacacagt gctcatcaaa aactattgct ccagctgtaa ttttaaatgt tggaggtggt 240
 tcaaaattct aaagagttat agaaataaca cacatttgac aaatacatat aaaaatagtt 300
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 atttgtgttg ctgacactg tccatctatt tttagaaac gtcttaaatg tcaactcaatg 420
 gggcaacttt cctggtttcc tatgtcttac cttagaagca agcagtgtgt tagaatggat 480
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<210> 116
 <211> 602
 <212> DNA
 <213> Human

<220>
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 <222> (294)..(294)
 <223> n is a, c, g, or t

<400> 116
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 aaaacaaaac accagactgc aacaataaca ggaaaagatc ctcttcagtg atttatgttg 180
 ttctcttact ttcataacta gtttgaatgc aaggctggta aaggatata cagagaatca 240
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 caggacaaga cattgcatgc ttggtcacag aactatcag cgagccagga attcgacat 420
 ccctgattac agtaagagac actgtttatt cctccaccaa actgccaggg ctgtccaact 480
 ccaatactcc cagtacctcc acctcctgca atatagcgac tccctccact gtttccagag 540

caatccccac catccaatc gcaggctgaa ttatttacag ccttgtcaca atagccatcc 600
 tt 602

<210> 117
 <211> 351
 <212> DNA
 <213> Human

<220>
 <221> misc_feature
 <222> (341)..(341)
 <223> n is a, c, g, or t

<400> 117
 tttttcggcc tcagtctgtt ctcagaacat actccatcac ctggttccca gaactcagat 60
 tgcgcagtgg tctcgtcatc atcggccagg actcacagtg cccgcggcag aggcctccct 120
 agacctccct ccggtccagc ctcacccgct gcctactctc ctcacgcccc tgctccaggt 180
 cccctggccc catttcgctc gccacgtttt cataatcctc tcaggctccg ggcaagcggc 240
 gcgcgccgca atgggacctg atcatataag gaaaatactg cgggctcatc cgggggctgc 300
 aatggtaacc cgaaagcgcc ctagcctact acaatcacccg naccocaaact g 351

<210> 118
 <211> 462
 <212> DNA
 <213> Human

<400> 118
 gctaagaaat aacttttatt aaaaatactg tgctagtact tatgcaatta cataatttta 60
 actaaatatt gtccactgcc acaattcgca ttaccaaact catattacca aatttttaggc 120
 cttgatagag cctaaatgct tcagtcactt cagaccaata acttaattct gttttcacat 180
 accttataca ctggcctacc aatagctctc aattcctgtc aatactttcc ccattctgca 240
 aaaagagggc cccatcccca tccctaataa aaaccaatgt gttgtacctg aaactgcaaa 300
 gattaatgct tttcgatgac cactaacttt tgaagccoga aggcctaact tttagacaac 360
 taaagctaca cactgttaaa attcttgggc ttctgtctta ttcagcaagc tgactcagta 420
 aaattaatac actgtatgaa aaaagctaac atacctacaa tc 462

<210> 119
 <211> 332
 <212> DNA
 <213> Human

<400> 119
 tttttttttt tttttttttt ttttggttta aaaataaatt ttttttatta catgataata 60
 ttgacagttt acataaacaa agttatttag tgtatgcaa gcaactataa aatacatttt 120
 gaaaagatat aaaaatcttt gaaattcttt cttgatatca gatctaccaa atttcgagag 180
 ccaccattga ttttttagga tcaaaacaaa atggcttgag agattttgtt ggtcagccaa 240
 actcagtcca ggaaaaaaga aacattaaag cattgttttg tgtttttaaa agctctaag 300
 gatattttatt ccaagctcct ttcgtatoga ag 332

<210> 120
 <211> 473
 <212> DNA
 <213> Human

<220>
 <221> misc_feature
 <222> (373)..(373)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (429)..(429)
 <223> n is a, c, g, or t

<400> 120
 ttttttttaa aatttcttcc agtttgggat tgtgtatata caaaaagctc aaaataaagc 60
 aactctgcaa tataatctta aaataatggc tactggggga aattctatca caaccattga 120
 aaataatggg gacttctcac ggagtctgtg gcatctgaga acccagttaa ttaaccaaag 180
 tcttgctcat attagcctca gttaccaga ttaaagcagg aactccggcc ttccttggac 240
 tgctgaaaac ccaacagatt ttctcaacat gctataagga aagagggaaa aattggtttc 300
 agctcacacc tcatgggctg ggaagcttct gggaaggcct ccaggccagt ggcacactcc 360
 ccaactttat ggntaaaagg aggggccaat tttcattccc cacaggcatt cacaaggagt 420
 tcccaccnt ccaaccacac agtggttttg gacaccaagg ttcacccttt cct 473

<210> 121
 <211> 525
 <212> DNA
 <213> Human

<400> 121
 gagaggatg ataatattt tttcttttcc atccaaatta tcagtaacag tggctaaatg 60
 gcaagatagg ctaaaaaact ctaagtacc caattttaca aattaaagaa gtaagtaaac 120
 attagaatga atacagttaa acaggagagg ctgggcacag tggctcacac ctgtaatccc 180

agtattatcc agtaaaagtt tagcaagcaa attcaaagaa gtctgttgtg caaccatagc 240
 cctttgcagt agaattctgct' atacagccta ttatgaggga tcaatttctt tctttcttct 300
 tttttttttg agacagagtc ttgtctgtt gcccaacctg gaatgcagtg gggatgattc 360
 ggctcactgc aacctctgcc tcccagggtc aagcaattct cctgtctcag cctcccagat 420
 agctggatta cagggtgtgca ccatcacacc cagctaattt ttgtattttt agtagagatg 480
 gggtttcacc acattgggtca ggctgggtctc aaactcctga cctca 525

<210> 122
 <211> 849
 <212> DNA
 <213> Human

<220>
 <221> misc_feature
 <222> (598)..(598)
 <223> n is a, c, g, or t

<400> 122
 atatgtatat ttctctctga ttttatgact gatttacaaa ttaggagtgc aaatgggctg 60
 ttccccgata gcatcttctg ggaagaatcc aaccaagata caaagcagat gatggtggat 120
 cggcaaaactc ttttctatga aaagaaaaac cagatatacc agggactgga aagcacctgc 180
 ttgaaaattg atatgagcat gtctgaattt ttcccttata agagcctgag tattgtaaca 240
 ggtctcttgc acaggggggt gaaaaataaa aaaagaagtt aacataatta aaatgcttgg 300
 acaaaacatt tgctttatat agattcttac aagtaattt tgattaggta tcaaaatagg 360
 tttaggcagg tggaagttct gaatttcaag gcaaataagg catgaagggt ggaacattgc 420
 atctagggaa aataagagaa ataagtgaat gtctgacctc acattgccaa ttctcagacc 480
 aagtacaaag tattaggaat tttttatata agctgacatc tttgtgctta cagtaaagcc 540
 atattagatg cacacatagt gactttatta aatcaaatga gtgtgcagag cagagcanat 600
 ctaattaggc tttctctttt agagttttct tattttactc ttattagctc cctccagttg 660
 gtcacatcaatt tcctatccta catcagatat ttacactatc agattctttg gtttaaaatc 720
 ctcttcgggt ttacatttta atttctgggg cgctaaacac atacttctgt cccggtctta 780
 tccctctatt ggaattcccc acagcgtggg caaaaacgcg ggctcgaaaa atggggggcc 840
 ccttccct 849

<210> 123
 <211> 454

<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (433)..(433)
<223> n is a, c, g, or t

<400> 123
ttgtgagcaa catcggtgtgt ttattcactt gtgtgtgagt gggctgagtc cgagaaaggg 60
gtcagcaaaa ggtggtggga ttatcattgg ttcttatagg ttgggatag gcggtgtagt 120
caggagcaat tttttacagg caggggatgg atattacaaa gtacattctc aaggggtggg 180
aggatgttac aaagtacatt cacaagggca gggaggggtgt atcgtcacaa gggcagggag 240
gatgtattgt cacaaggggtg gggaggaatg ttacaaagta cattcacaag gacaggagta 300
tcacaaagta cattatcaca aggggtggggg aatgtcaccg tggcttgacc attagtgcag 360
ccagctccag aggaccttac caaaaagttt ccatacttgc acgtgttttc ctggtggcca 420
aaaatataaa acntttaatt tctgggattc cttt 454

<210> 124
<211> 485
<212> DNA
<213> Human

<400> 124
ttcagatttg acatgtcaat ctttatttaa gacaacaaaa gtttgtacac tctcatatta 60
agatatattt cttttctagt catattaaaa taatctcatt ttgttactca aaaagaatac 120
ataggaaga gaatgaacat aattcaagta gatagatttc taattgggta aaacaggggt 180
aaacaaatga tgttcaaaat atacttatta aagggaacag cacctagaaa taggcagtag 240
ggcaatgttc actttaagaa ttttatcaat aactagggca aagaacaaaa tcattatcaa 300
attttgaatt acacaaaagc aatggcctat taccttggtta acatttgata tttctatata 360
tcttcttctc tagttgaaat gggtaatgac ttgtattaca aggatgttac acattctaaa 420
atgatttaag ccaaaagatt atctttaata cattacttct agatataata tgtacttgat 480
gtctg 485

<210> 125
<211> 558
<212> DNA
<213> Human

<400> 125
ttttcagaca tgacagcatt tgacacactc ccttttaatt tattgcagaa ataatatgaa 60


```

catctgggaa aatgatagtg ctaaatatct cgtgaagtaa gtcattctta gaaagggatt    120
tgtgactttg aagtaatata taattagcaa gatttttaaaa attattctta tgtactgaaa    180
ctcaaaacag actagcaaag tacctccaaa aaaaaaacta tcaaattaaa ctagaaaagt    240
atttccaaaa taaagacgac caaaaactag cctgagaata ctagttttct gttgctacaa    300
cacattacca caaacttagt ggcttaaaca caaatctatt atcttacagt tctgcagatt    360
agaggtccaa cacaggcttc actgggctaa aatcaagggtg ttggcagggc tgcgttcctt    420
ctgggagggt atggggaagt ttctgtttcc tttccagtct caattctacc ggctgcctgc    480
aactccctgg cttatggccc cttctccat cttcaaagcc aggaatgggt catccctctc    540
taagcgttct ccctattt                                                    558

```

<210> 126
 <211> 508
 <212> PRT
 <213> Human

<400> 126

```

Met Gln Arg Leu Leu Thr Pro Val Lys Arg Ile Leu Gln Leu Thr Arg
1           5           10           15

```

```

Ala Val Gln Glu Thr Ser Leu Thr Pro Ala Arg Leu Leu Pro Val Ala
          20           25           30

```

```

His Gln Arg Phe Ser Thr Ala Ser Ala Val Pro Leu Ala Lys Thr Asp
          35           40           45

```

```

Thr Trp Pro Lys Asp Val Gly Ile Leu Ala Leu Glu Val Tyr Phe Pro
          50           55           60

```

```

Ala Gln Tyr Val Asp Gln Thr Asp Leu Glu Lys Tyr Asn Asn Val Glu
65           70           75           80

```

```

Ala Gly Lys Tyr Thr Val Gly Leu Gly Gln Thr Arg Met Gly Phe Cys
          85           90           95

```

```

Ser Val Gln Glu Asp Ile Asn Ser Leu Cys Leu Thr Val Val Gln Arg
          100          105          110

```

```

Leu Met Glu Arg Ile Gln Leu Pro Trp Asp Ser Val Gly Arg Leu Glu
          115          120          125

```

Val Gly Thr Glu Thr Ile Ile Asp Lys Ser Lys Ala Val Lys Thr Val
 130 135 140

Leu Met Glu Leu Phe Gln Asp Ser Gly Asn Thr Asp Ile Glu Gly Ile
 145 150 155 160

Asp Thr Thr Asn Ala Cys Tyr Gly Gly Thr Ala Ser Leu Phe Asn Ala
 165 170 175

Ala Asn Trp Met Glu Ser Ser Ser Trp Asp Gly Arg Tyr Ala Met Val
 180 185 190

Val Cys Gly Asp Ile Ala Val Tyr Pro Ser Gly Asn Ala Arg Pro Thr
 195 200 205

Gly Gly Ala Gly Ala Val Ala Met Leu Ile Gly Pro Lys Ala Pro Leu
 210 215 220

Ala Leu Glu Arg Gly Leu Arg Gly Thr His Met Glu Asn Val Tyr Asp
 225 230 235 240

Phe Tyr Lys Pro Asn Leu Ala Ser Glu Tyr Pro Ile Val Asp Gly Lys
 245 250 255

Leu Ser Ile Gln Cys Tyr Leu Arg Ala Leu Asp Arg Cys Tyr Thr Ser
 260 265 270

Tyr Arg Lys Lys Ile Gln Asn Gln Trp Lys Gln Ala Gly Ser Asp Arg
 275 280 285

Pro Phe Thr Leu Asp Asp Leu Gln Tyr Met Ile Phe His Thr Pro Phe
 290 295 300

Cys Lys Met Val Gln Lys Ser Leu Ala Arg Leu Met Phe Asn Asp Phe
 305 310 315 320

Leu Ser Ala Ser Ser Asp Thr Gln Thr Ser Leu Tyr Lys Gly Leu Glu
 325 330 335

Ala Phe Gly Gly Leu Lys Leu Glu Asp Thr Tyr Thr Asn Lys Asp Leu
 340 345 350

Asp Lys Ala Leu Leu Lys Ala Ser Gln Asp Met Phe Asp Lys Lys Thr
 355 360 365

Lys Ala Ser Leu Tyr Leu Ser Thr His Asn Gly Asn Met Tyr Thr Ser
370 375 380

Ser Leu Tyr Gly Cys Leu Ala Ser Leu Leu Ser His His Ser Ala Gln
385 390 395 400

Glu Leu Ala Gly Ser Arg Ile Gly Ala Phe Ser Tyr Gly Ser Gly Leu
405 410 415

Ala Ala Ser Phe Phe Ser Phe Arg Val Ser Gln Asp Ala Ala Pro Gly
420 425 430

Ser Pro Leu Asp Lys Leu Val Ser Ser Thr Ser Asp Leu Pro Lys Arg
435 440 445

Leu Ala Ser Arg Lys Cys Val Ser Pro Glu Glu Phe Thr Glu Ile Met
450 455 460

Asn Gln Arg Glu Gln Phe Tyr His Lys Val Asn Phe Ser Pro Pro Gly
465 470 475 480

Asp Thr Asn Ser Leu Phe Pro Gly Thr Trp Tyr Leu Glu Arg Val Asp
485 490 495

Glu Gln His Arg Arg Lys Tyr Ala Arg Arg Pro Val
500 505

<210> 127
<211> 396
<212> PRT
<213> Human

<400> 127

Met Val Ala Gly Thr Arg Cys Leu Leu Ala Leu Leu Leu Pro Gln Val
1 5 10 15

Leu Leu Gly Gly Ala Ala Gly Leu Val Pro Glu Leu Gly Arg Arg Lys
20 25 30

Phe Ala Ala Ala Ser Ser Gly Arg Pro Ser Ser Gln Pro Ser Asp Glu
35 40 45

Val Leu Ser Glu Phe Glu Leu Arg Leu Leu Ser Met Phe Gly Leu Lys
50 55 60

Gln Arg Pro Thr Pro Ser Arg Asp Ala Val Val Pro Pro Tyr Met Leu
 65 70 75 80

Asp Leu Tyr Arg Arg His Ser Gly Gln Pro Gly Ser Pro Ala Pro Asp
 85 90 95

His Arg Leu Glu Arg Ala Ala Ser Arg Ala Asn Thr Val Arg Ser Phe
 100 105 110

His His Glu Glu Ser Leu Glu Glu Leu Pro Glu Thr Ser Gly Lys Thr
 115 120 125

Thr Arg Arg Phe Phe Phe Asn Leu Ser Ser Ile Pro Thr Glu Glu Phe
 130 135 140

Ile Thr Ser Ala Glu Leu Gln Val Phe Arg Glu Gln Met Gln Asp Ala
 145 150 155 160

Leu Gly Asn Asn Ser Ser Phe His His Arg Ile Asn Ile Tyr Glu Ile
 165 170 175

Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe Pro Val Thr Arg Leu Leu
 180 185 190

Asp Thr Arg Leu Val Asn Gln Asn Ala Ser Arg Trp Glu Ser Phe Asp
 195 200 205

Val Thr Pro Ala Val Met Arg Trp Thr Ala Gln Gly His Ala Asn His
 210 215 220

Gly Phe Val Val Glu Val Ala His Leu Glu Glu Lys Gln Gly Val Ser
 225 230 235 240

Lys Arg His Val Arg Ile Ser Arg Ser Leu His Gln Asp Glu His Ser
 245 250 255

Trp Ser Gln Ile Arg Pro Leu Leu Val Thr Phe Gly His Asp Gly Lys
 260 265 270

Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His Lys Gln
 275 280 285

Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr Val Asp
 290 295 300

Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr
305 310 315 320

His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His
325 330 335

Leu Asn Ser Thr Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val
340 345 350

Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala
355 360 365

Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu Lys Val Val Leu Lys Asn
370 375 380

Tyr Gln Asp Met Val Val Glu Gly Cys Gly Cys Arg
385 390 395

<210> 128
<211> 219
<212> PRT
<213> Human

<400> 128

Met Ala Asp Lys Ala Lys Pro Ala Lys Ala Ala Asn Arg Thr Pro Pro
1 5 10 15

Lys Ser Pro Gly Asp Pro Ser Lys Asp Arg Ala Ala Lys Arg Leu Ser
20 25 30

Leu Glu Ser Glu Gly Ala Gly Glu Gly Ala Ala Ala Ser Pro Glu Leu
35 40 45

Ser Ala Leu Glu Glu Ala Phe Arg Arg Phe Ala Val His Gly Asp Ala
50 55 60

Arg Ala Thr Gly Arg Glu Met His Gly Lys Asn Trp Ser Lys Leu Cys
65 70 75 80

Lys Asp Cys Gln Val Ile Asp Gly Arg Asn Val Thr Val Thr Asp Val
85 90 95

Asp Ile Val Phe Ser Lys Ile Lys Gly Lys Ser Cys Arg Thr Ile Thr
100 105 110

Phe Glu Gln Phe Gln Glu Ala Leu Glu Glu Leu Ala Lys Lys Arg Phe
 115 120 125

Lys Asp Lys Ser Ser Glu Glu Ala Val Arg Glu Val His Arg Leu Ile
 130 135 140

Glu Gly Lys Ala Pro Ile Ile Ser Gly Val Thr Lys Ala Ile Ser Ser
 145 150 155 160

Pro Thr Val Ser Arg Leu Thr Asp Thr Thr Lys Phe Thr Gly Ser His
 165 170 175

Lys Glu Arg Phe Asp Pro Ser Gly Lys Gly Lys Gly Lys Ala Gly Arg
 180 185 190

Val Asp Leu Val Asp Glu Ser Gly Tyr Val Ser Gly Tyr Lys His Ala
 195 200 205

Gly Thr Tyr Asp Gln Lys Val Gln Gly Gly Lys
 210 215

<210> 129
 <211> 384
 <212> PRT
 <213> Human

<400> 129

Met Asp Cys Ser Asn Gly Ser Ala Glu Cys Thr Gly Glu Gly Gly Ser
 1 5 10 15

Lys Glu Val Val Gly Thr Phe Lys Ala Lys Asp Leu Ile Val Thr Pro
 20 25 30

Ala Thr Ile Leu Lys Glu Lys Pro Asp Pro Asn Asn Leu Val Phe Gly
 35 40 45

Thr Val Phe Thr Asp His Met Leu Thr Val Glu Trp Ser Ser Glu Phe
 50 55 60

Gly Trp Glu Lys Pro His Ile Lys Pro Leu Gln Asn Leu Ser Leu His
 65 70 75 80

Pro Gly Ser Ser Ala Leu His Tyr Ala Val Glu Leu Phe Glu Gly Leu
 85 90 95

Lys Ala Phe Arg Gly Val Asp Asn Lys Ile Arg Leu Phe Gln Pro Asn
 100 105 110

Leu Asn Met Asp Arg Met Tyr Arg Ser Ala Val Arg Ala Thr Leu Pro
 115 120 125

Val Phe Asp Lys Glu Glu Leu Leu Glu Cys Ile Gln Gln Leu Val Lys
 130 135 140

Leu Asp Gln Glu Trp Val Pro Tyr Ser Thr Ser Ala Ser Leu Tyr Ile
 145 150 155 160

Arg Pro Ala Phe Ile Gly Thr Glu Pro Ser Leu Gly Val Lys Lys Pro
 165 170 175

Thr Lys Ala Leu Leu Phe Val Leu Leu Ser Pro Val Gly Pro Tyr Phe
 180 185 190

Ser Ser Gly Thr Phe Asn Pro Val Ser Leu Trp Ala Asn Pro Lys Tyr
 195 200 205

Val Arg Ala Trp Lys Gly Gly Thr Gly Asp Cys Lys Met Gly Gly Asn
 210 215 220

Tyr Gly Ser Ser Leu Phe Ala Gln Cys Glu Asp Val Asp Asn Gly Cys
 225 230 235 240

Gln Gln Val Leu Trp Leu Tyr Gly Arg Asp His Gln Ile Thr Glu Val
 245 250 255

Gly Thr Met Asn Leu Phe Leu Tyr Trp Ile Asn Glu Asp Gly Glu Glu
 260 265 270

Glu Leu Ala Thr Pro Pro Leu Asp Gly Ile Ile Leu Pro Gly Val Thr
 275 280 285

Arg Arg Cys Ile Leu Asp Leu Ala His Gln Trp Gly Glu Phe Lys Val
 290 295 300

Ser Glu Arg Tyr Leu Thr Met Asp Asp Leu Thr Thr Ala Leu Glu Gly
 305 310 315 320

Asn Arg Val Arg Glu Met Phe Ser Ser Gly Thr Ala Cys Val Val Cys

297/439

145

150

155

<210> 131
 <211> 344
 <212> PRT
 <213> Human

<400> 131

Met Gly Pro Pro Ser Ala Pro Pro Cys Arg Leu His Val Pro Trp Lys
 1 5 10 15

Glu Val Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr
 20 25 30

Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
 35 40 45

Lys Glu Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly
 50 55 60

Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val
 65 70 75 80

Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser
 85 90 95

Gly Arg Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val
 100 105 110

Thr Gln Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp
 115 120 125

Leu Val Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu
 130 135 140

Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Asn Pro Val Glu Asp Lys
 145 150 155 160

Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Val Gln Asn Thr Thr Tyr
 165 170 175

Leu Trp Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Arg Leu Gln
 180 185 190

Leu Ser Asn Gly Asn Met Thr Leu Thr Leu Leu Ser Val Lys Arg Asn

195 200 205
 Asp Ala Gly Ser Tyr Glu Cys Glu Ile Gln Asn Pro Ala Ser Ala Asn
 210 215 220
 Arg Ser Asp Pro Val Thr Leu Asn Val Leu Tyr Gly Pro Asp Val Pro
 225 230 235 240
 Thr Ile Ser Pro Ser Lys Ala Asn Tyr Arg Pro Gly Glu Asn Leu Asn
 245 250 255
 Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser Trp Phe
 260 265 270
 Ile Asn Gly Thr Phe Gln Gln Ser Thr Gln Glu Leu Phe Ile Pro Asn
 275 280 285
 Ile Thr Val Asn Asn Ser Gly Ser Tyr Met Cys Gln Ala His Asn Ser
 290 295 300
 Ala Thr Gly Leu Asn Arg Thr Thr Val Thr Met Ile Thr Val Ser Gly
 305 310 315 320
 Ser Ala Pro Val Leu Ser Ala Val Ala Thr Val Gly Ile Thr Ile Gly
 325 330 335
 Val Leu Ala Arg Val Ala Leu Ile
 340
 <210> 132
 <211> 479
 <212> PRT
 <213> Human
 <400> 132
 Met Lys Ser Gln Gly Gln His Trp Tyr Ser Ser Ser Asp Lys Asn Cys
 1 5 10 15
 Lys Val Ser Phe Arg Glu Lys Leu Leu Ile Ile Asp Ser Asn Leu Gly
 20 25 30
 Val Gln Asp Val Glu Asn Leu Lys Phe Leu Cys Ile Gly Leu Val Pro
 35 40 45
 Asn Lys Lys Leu Glu Lys Ser Ser Ser Ala Ser Asp Val Phe Glu His

50		55		60
Leu Leu Ala Glu Asp	Leu Leu Ser Glu Glu Asp	Pro Phe Phe Leu Ala		
65	70	75	80	
Glu Leu Leu Tyr Ile	Ile Arg Gln Lys Lys Leu Leu Gln His	Leu Asn		
	85	90	95	
Cys Thr Lys Glu Glu Val	Glu Arg Leu Leu Pro Thr Arg	Gln Arg Val		
	100	105	110	
Ser Leu Phe Arg Asn	Leu Leu Tyr Glu Leu Ser Glu Gly Ile Asp	Ser		
	115	120	125	
Glu Asn Leu Lys Asp Met	Ile Phe Leu Leu Lys Asp Ser Leu Pro Lys			
	130	135	140	
Thr Glu Met Thr Ser	Leu Ser Phe Leu Ala Phe Leu Glu Lys Gln Gly			
	145	150	155	160
Lys Ile Asp Glu Asp	Asn Leu Thr Cys Leu Glu Asp Leu Cys Lys Thr			
	165	170	175	
Val Val Pro Lys Leu Leu Arg	Asn Ile Glu Lys Tyr Lys Arg Glu Lys			
	180	185	190	
Ala Ile Gln Ile Val Thr	Pro Pro Val Asp Lys Glu Ala Glu Ser Tyr			
	195	200	205	
Gln Gly Glu Glu Glu Leu	Val Ser Gln Thr Asp Val Lys Thr Phe Leu			
	210	215	220	
Glu Ala Leu Pro Arg	Ala Ala Val Tyr Arg Met Asn Arg Asn His Arg			
	225	230	235	240
Gly Leu Cys Val Ile	Val Asn Asn His Ser Phe Thr Ser Leu Lys Asp			
	245	250	255	
Arg Gln Gly Thr His	Lys Asp Ala Glu Ile Leu Ser His Val Phe Gln			
	260	265	270	
Trp Leu Gly Phe Thr	Val His Ile His Asn Asn Val Thr Lys Val Glu			
	275	280	285	

Met Glu Met Val Leu Gln Lys Gln Lys Cys Asn Pro Ala His Ala Asp
 290 295 300

Gly Asp Cys Phe Val Phe Cys Ile Leu Thr His Gly Arg Phe Gly Ala
 305 310 315 320

Val Tyr Ser Ser Asp Glu Ala Leu Ile Pro Ile Arg Glu Ile Met Ser
 325 330 335

His Phe Thr Ala Leu Gln Cys Pro Arg Leu Ala Glu Lys Pro Lys Leu
 340 345 350

Phe Phe Ile Gln Ala Cys Gln Gly Glu Glu Ile Gln Pro Ser Val Ser
 355 360 365

Ile Glu Ala Asp Ala Leu Asn Pro Glu Gln Ala Pro Thr Ser Leu Gln
 370 375 380

Asp Ser Ile Pro Ala Glu Ala Asp Phe Leu Leu Gly Leu Ala Thr Val
 385 390 395 400

Pro Gly Tyr Val Ser Phe Arg His Val Glu Glu Gly Ser Trp Tyr Ile
 405 410 415

Gln Ser Leu Cys Asn His Leu Lys Lys Leu Val Pro Arg His Glu Asp
 420 425 430

Ile Leu Ser Ile Leu Thr Ala Val Asn Asp Asp Val Ser Arg Arg Val
 435 440 445

Asp Lys Gln Gly Thr Lys Lys Gln Met Pro Gln Pro Ala Phe Thr Leu
 450 455 460

Arg Lys Lys Leu Val Phe Pro Val Pro Leu Asp Ala Leu Ser Ile
 465 470 475

<210> 133
 <211> 509
 <212> PRT
 <213> Human

<400> 133

Met Thr Val Glu Gly Arg Leu Leu Val Pro Asp Arg Ile Asn Gly Thr
 1 5 10 15

Ala Asn Lys Met Asn Gly Ala Leu Asp His Ser Asp Gln Pro Asp Pro
 20 25 30

Asp Ala Ile Lys Met Phe Val Gly Gln Ile Pro Arg Ser Trp Ser Glu
 35 40 45

Lys Glu Leu Lys Glu Leu Phe Glu Pro Tyr Gly Ala Val Tyr Gln Ile
 50 55 60

Asn Val Leu Arg Asp Arg Ser Gln Asn Pro Pro Gln Ser Lys Gly Cys
 65 70 75 80

Cys Phe Val Thr Phe Tyr Thr Arg Lys Ala Ala Leu Glu Ala Gln Asn
 85 90 95

Ala Leu His Asn Ile Lys Thr Leu Pro Gly Met His His Pro Ile Gln
 100 105 110

Met Lys Pro Ala Asp Ser Glu Lys Ser Asn Ala Val Glu Asp Arg Lys
 115 120 125

Leu Phe Ile Gly Met Val Ser Lys Lys Cys Asn Glu Asn Asp Ile Arg
 130 135 140

Val Met Phe Ser Pro Phe Gly Gln Ile Glu Glu Cys Arg Ile Leu Arg
 145 150 155 160

Gly Pro Asp Gly Leu Ser Arg Gly Cys Ala Phe Val Thr Phe Ser Thr
 165 170 175

Arg Ala Met Ala Gln Asn Ala Ile Lys Ala Met His Gln Ser Gln Thr
 180 185 190

Met Glu Gly Cys Ser Ser Pro Ile Val Val Lys Phe Ala Asp Thr Gln
 195 200 205

Lys Asp Lys Glu Gln Arg Arg Leu Gln Gln Gln Leu Ala Gln Gln Met
 210 215 220

Gln Gln Leu Asn Thr Ala Thr Trp Gly Asn Leu Thr Gly Leu Gly Gly
 225 230 235 240

Leu Thr Pro Gln Tyr Leu Ala Leu Leu Gln Gln Ala Thr Ser Ser Ser
 245 250 255

Asn Leu Gly Ala Phe Ser Gly Ile Gln Gln Met Ala Gly Met Asn Ala
 260 265 270

Leu Gln Leu Gln Asn Leu Ala Thr Leu Ala Ala Ala Ala Ala Ala
 275 280 285

Gln Thr Ser Ala Thr Ser Thr Asn Ala Asn Pro Leu Ser Thr Thr Ser
 290 295 300

Ser Ala Leu Gly Ala Leu Thr Ser Pro Val Ala Ala Ser Thr Pro Asn
 305 310 315 320

Ser Thr Ala Gly Ala Ala Met Asn Ser Leu Thr Ser Leu Gly Thr Leu
 325 330 335

Gln Gly Leu Ala Gly Ala Thr Val Gly Leu Asn Asn Ile Asn Ala Leu
 340 345 350

Ala Val Ala Gln Met Leu Ser Gly Met Ala Ala Leu Asn Gly Gly Leu
 355 360 365

Gly Ala Thr Gly Leu Thr Asn Gly Thr Ala Gly Thr Met Asp Ala Leu
 370 375 380

Thr Gln Ala Tyr Ser Gly Ile Gln Gln Tyr Ala Ala Ala Ala Leu Pro
 385 390 395 400

Thr Leu Tyr Ser Gln Ser Leu Leu Gln Gln Gln Ser Ala Ala Gly Ser
 405 410 415

Gln Lys Glu Gly Pro Glu Gly Ala Asn Leu Phe Ile Tyr His Leu Pro
 420 425 430

Gln Glu Phe Gly Asp Gln His Ile Leu Gln Met Phe Met Pro Phe Gly
 435 440 445

Asn Val Ile Ser Ala Lys Val Phe Ile Asp Lys Gln Thr Asn Leu Ser
 450 455 460

Lys Cys Phe Gly Phe Val Ser Tyr Asp Asn Pro Val Ser Ala Gln Ala
 465 470 475 480

Ala Ile Gln Ala Met Asn Gly Phe Gln Ile Gly Met Lys Arg Leu Lys
 485 490 495

Val Gln Leu Lys Arg Ser Lys Asn Asp Ser Lys Pro Tyr
 500 505

<210> 134
 <211> 141
 <212> PRT
 <213> Human

<400> 134

Met Ala Arg Pro Leu Cys Thr Leu Leu Leu Leu Met Ala Thr Leu Ala
 1 5 10 15

Gly Ala Leu Ala Ser Ser Ser Lys Glu Glu Asn Arg Ile Ile Pro Gly
 20 25 30

Gly Ile Tyr Asp Ala Asp Leu Asn Asp Glu Trp Val Gln Arg Ala Leu
 35 40 45

His Phe Ala Ile Ser Glu Tyr Asn Lys Ala Thr Glu Asp Glu Tyr Tyr
 50 55 60

Arg Arg Pro Leu Gln Val Leu Arg Ala Arg Glu Gln Thr Phe Gly Gly
 65 70 75 80

Val Asn Tyr Phe Phe Asp Val Glu Val Gly Arg Thr Ile Cys Thr Lys
 85 90 95

Ser Gln Pro Asn Leu Asp Thr Cys Ala Phe His Glu Gln Pro Glu Leu
 100 105 110

Gln Lys Lys Gln Leu Cys Ser Phe Glu Ile Tyr Glu Val Pro Trp Glu
 115 120 125

Asp Arg Met Ser Leu Val Asn Ser Arg Cys Gln Glu Ala
 130 135 140

<210> 135
 <211> 1480
 <212> PRT
 <213> Human

<400> 135

Met Gln Arg Ser Pro Leu Glu Lys Ala Ser Val Val Ser Lys Leu Phe
 1 5 10 15

Phe Ser Trp Thr Arg Pro Ile Leu Arg Lys Gly Tyr Arg Gln Arg Leu
 20 25 30

Glu Leu Ser Asp Ile Tyr Gln Ile Pro Ser Val Asp Ser Ala Asp Asn
 35 40 45

Leu Ser Glu Lys Leu Glu Arg Glu Trp Asp Arg Glu Leu Ala Ser Lys
 50 55 60

Lys Asn Pro Lys Leu Ile Asn Ala Leu Arg Arg Cys Phe Phe Trp Arg
 65 70 75 80

Phe Met Phe Tyr Gly Ile Phe Leu Tyr Leu Gly Glu Val Thr Lys Ala
 85 90 95

Val Gln Pro Leu Leu Leu Gly Arg Ile Ile Ala Ser Tyr Asp Pro Asp
 100 105 110

Asn Lys Glu Glu Arg Ser Ile Ala Ile Tyr Leu Gly Ile Gly Leu Cys
 115 120 125

Leu Leu Phe Ile Val Arg Thr Leu Leu Leu His Pro Ala Ile Phe Gly
 130 135 140

Leu His His Ile Gly Met Gln Met Arg Ile Ala Met Phe Ser Leu Ile
 145 150 155 160

Tyr Lys Lys Thr Leu Lys Leu Ser Ser Arg Val Leu Asp Lys Ile Ser
 165 170 175

Ile Gly Gln Leu Val Ser Leu Leu Ser Asn Asn Leu Asn Lys Phe Asp
 180 185 190

Glu Gly Leu Ala Leu Ala His Phe Val Trp Ile Ala Pro Leu Gln Val
 195 200 205

Ala Leu Leu Met Gly Leu Ile Trp Glu Leu Leu Gln Ala Ser Ala Phe
 210 215 220

Cys Gly Leu Gly Phe Leu Ile Val Leu Ala Leu Phe Gln Ala Gly Leu
 225 230 235 240

Gly Arg Met Met Met Lys Tyr Arg Asp Gln Arg Ala Gly Lys Ile Ser
 245 250 255

Glu Arg Leu Val Ile Thr Ser Glu Met Ile Glu Asn Ile Gln Ser Val
 260 265 270

Lys Ala Tyr Cys Trp Glu Glu Ala Met Glu Lys Met Ile Glu Asn Leu
 275 280 285

Arg Gln Thr Glu Leu Lys Leu Thr Arg Lys Ala Ala Tyr Val Arg Tyr
 290 295 300

Phe Asn Ser Ser Ala Phe Phe Phe Ser Gly Phe Phe Val Val Phe Leu
 305 310 315 320

Ser Val Leu Pro Tyr Ala Leu Ile Lys Gly Ile Ile Leu Arg Lys Ile
 325 330 335

Phe Thr Thr Ile Ser Phe Cys Ile Val Leu Arg Met Ala Val Thr Arg
 340 345 350

Gln Phe Pro Trp Ala Val Gln Thr Trp Tyr Asp Ser Leu Gly Ala Ile
 355 360 365

Asn Lys Ile Gln Asp Phe Leu Gln Lys Gln Glu Tyr Lys Thr Leu Glu
 370 375 380

Tyr Asn Leu Thr Thr Thr Glu Val Val Met Glu Asn Val Thr Ala Phe
 385 390 395 400

Trp Glu Glu Gly Phe Gly Glu Leu Phe Glu Lys Ala Lys Gln Asn Asn
 405 410 415

Asn Asn Arg Lys Thr Ser Asn Gly Asp Asp Ser Leu Phe Phe Ser Asn
 420 425 430

Phe Ser Leu Leu Gly Thr Pro Val Leu Lys Asp Ile Asn Phe Lys Ile
 435 440 445

Glu Arg Gly Gln Leu Leu Ala Val Ala Gly Ser Thr Gly Ala Gly Lys
 450 455 460

Thr Ser Leu Leu Met Met Ile Met Gly Glu Leu Glu Pro Ser Glu Gly
 465 470 475 480

Lys Ile Lys His Ser Gly Arg Ile Ser Phe Cys Ser Gln Phe Ser Trp

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Met Asn Gly Ile Glu Glu Asp Ser Asp Glu Pro Leu Glu Arg Arg Leu
 725 730 735

Ser Leu Val Pro Asp Ser Glu Gln Gly Glu Ala Ile Leu Pro Arg Ile
 740 745 750

Ser Val Ile Ser Thr Gly Pro Thr Leu Gln Ala Arg Arg Arg Gln Ser
 755 760 765

Val Leu Asn Leu Met Thr His Ser Val Asn Gln Gly Gln Asn Ile His
 770 775 780

Arg Lys Thr Thr Ala Ser Thr Arg Lys Val Ser Leu Ala Pro Gln Ala
 785 790 795 800

Asn Leu Thr Glu Leu Asp Ile Tyr Ser Arg Arg Leu Ser Gln Glu Thr
 805 810 815

Gly Leu Glu Ile Ser Glu Glu Ile Asn Glu Glu Asp Leu Lys Glu Cys
 820 825 830

Leu Phe Asp Asp Met Glu Ser Ile Pro Ala Val Thr Thr Trp Asn Thr
 835 840 845

Tyr Leu Arg Tyr Ile Thr Val His Lys Ser Leu Ile Phe Val Leu Ile
 850 855 860

Trp Cys Leu Val Ile Phe Leu Ala Glu Val Ala Ala Ser Leu Val Val
 865 870 875 880

Leu Trp Leu Leu Gly Asn Thr Pro Leu Gln Asp Lys Gly Asn Ser Thr
 885 890 895

His Ser Arg Asn Asn Ser Tyr Ala Val Ile Ile Thr Ser Thr Ser Ser
 900 905 910

Tyr Tyr Val Phe Tyr Ile Tyr Val Gly Val Ala Asp Thr Leu Leu Ala
 915 920 925

Met Gly Phe Phe Arg Gly Leu Pro Leu Val His Thr Leu Ile Thr Val
 930 935 940

Ser Lys Ile Leu His His Lys Met Leu His Ser Val Leu Gln Ala Pro
 945 950 955 960

Met Ser Thr Leu Asn Thr Leu Lys Ala Gly Gly Ile Leu Asn Arg Phe
 965 970 975

Ser Lys Asp Ile Ala Ile Leu Asp Asp Leu Leu Pro Leu Thr Ile Phe
 980 985 990

Asp Phe Ile Gln Leu Leu Leu Ile Val Ile Gly Ala Ile Ala Val Val
 995 1000 1005

Ala Val Leu Gln Pro Tyr Ile Phe Val Ala Thr Val Pro Val Ile
 1010 1015 1020

Val Ala Phe Ile Met Leu Arg Ala Tyr Phe Leu Gln Thr Ser Gln
 1025 1030 1035

Gln Leu Lys Gln Leu Glu Ser Glu Gly Arg Ser Pro Ile Phe Thr
 1040 1045 1050

His Leu Val Thr Ser Leu Lys Gly Leu Trp Thr Leu Arg Ala Phe
 1055 1060 1065

Gly Arg Gln Pro Tyr Phe Glu Thr Leu Phe His Lys Ala Leu Asn
 1070 1075 1080

Leu His Thr Ala Asn Trp Phe Leu Tyr Leu Ser Thr Leu Arg Trp
 1085 1090 1095

Phe Gln Met Arg Ile Glu Met Ile Phe Val Ile Phe Phe Ile Ala
 1100 1105 1110

Val Thr Phe Ile Ser Ile Leu Thr Thr Gly Glu Gly Glu Gly Arg
 1115 1120 1125

Val Gly Ile Ile Leu Thr Leu Ala Met Asn Ile Met Ser Thr Leu
 1130 1135 1140

Gln Trp Ala Val Asn Ser Ser Ile Asp Val Asp Ser Leu Met Arg
 1145 1150 1155

Ser Val Ser Arg Val Phe Lys Phe Ile Asp Met Pro Thr Glu Gly
 1160 1165 1170

Lys Pro Thr Lys Ser Thr Lys Pro Tyr Lys Asn Gly Gln Leu Ser
 1175 1180 1185

Lys Val	Met Ile Ile	Glu Asn	Ser His Val	Lys Lys	Asp Asp Ile
1190		1195		1200	
Trp Pro	Ser Gly Gly	Gln Met	Thr Val Lys	Asp Leu	Thr Ala Lys
1205		1210		1215	
Tyr Thr	Glu Gly Gly	Asn Ala	Ile Leu Glu	Asn Ile	Ser Phe Ser
1220		1225		1230	
Ile Ser	Pro Gly Gln	Arg Val	Gly Leu Leu	Gly Arg	Thr Gly Ser
1235		1240		1245	
Gly Lys	Ser Thr Leu	Leu Ser	Ala Phe Leu	Arg Leu	Leu Asn Thr
1250		1255		1260	
Glu Gly	Glu Ile Gln	Ile Asp	Gly Val Ser	Trp Asp	Ser Ile Thr
1265		1270		1275	
Leu Gln	Gln Trp Arg	Lys Ala	Phe Gly Val	Ile Pro	Gln Lys Val
1280		1285		1290	
Phe Ile	Phe Ser Gly	Thr Phe	Arg Lys Asn	Leu Asp	Pro Tyr Glu
1295		1300		1305	
Gln Trp	Ser Asp Gln	Glu Ile	Trp Lys Val	Ala Asp	Glu Val Gly
1310		1315		1320	
Leu Arg	Ser Val Ile	Glu Gln	Phe Pro Gly	Lys Leu	Asp Phe Val
1325		1330		1335	
Leu Val	Asp Gly Gly	Cys Val	Leu Ser His	Gly His	Lys Gln Leu
1340		1345		1350	
Met Cys	Leu Ala Arg	Ser Val	Leu Ser Lys	Ala Lys	Ile Leu Leu
1355		1360		1365	
Leu Asp	Glu Pro Ser	Ala His	Leu Asp Pro	Val Thr	Tyr Gln Ile
1370		1375		1380	
Ile Arg	Arg Thr Leu	Lys Gln	Ala Phe Ala	Asp Cys	Thr Val Ile
1385		1390		1395	
Leu Cys	Glu His Arg	Ile Glu	Ala Met Leu	Glu Cys	Gln Gln Phe

1400 1405 1410
 Leu Val Ile Glu Glu Asn Lys Val Arg Gln Tyr Asp Ser Ile Gln
 1415 1420 1425
 Lys Leu Leu Asn Glu Arg Ser Leu Phe Arg Gln Ala Ile Ser Pro
 1430 1435 1440
 Ser Asp Arg Val Lys Leu Phe Pro His Arg Asn Ser Ser Lys Cys
 1445 1450 1455
 Lys Ser Lys Pro Gln Ile Ala Ala Leu Lys Glu Glu Thr Glu Glu
 1460 1465 1470
 Glu Val Gln Asp Thr Arg Leu
 1475 1480

 <210> 136
 <211> 502
 <212> PRT
 <213> Human

 <400> 136
 Met Leu Ala Ala Met Gly Ser Leu Ala Ala Ala Leu Trp Ala Val Val
 1 5 10 15
 His Pro Arg Thr Leu Leu Leu Gly Thr Val Ala Phe Leu Leu Ala Ala
 20 25 30
 Asp Phe Leu Lys Arg Arg Arg Pro Lys Asn Tyr Pro Pro Gly Pro Trp
 35 40 45
 Arg Leu Pro Phe Leu Gly Asn Phe Phe Leu Val Asp Phe Glu Gln Ser
 50 55 60
 His Leu Glu Val Gln Leu Phe Val Lys Lys Tyr Gly Asn Leu Phe Ser
 65 70 75 80
 Leu Glu Leu Gly Asp Ile Ser Ala Val Leu Ile Thr Gly Leu Pro Leu
 85 90 95
 Ile Lys Glu Ala Leu Ile His Met Asp Gln Asn Phe Gly Asn Arg Pro
 100 105 110
 Val Thr Pro Met Arg Glu His Ile Phe Lys Lys Asn Gly Leu Ile Met

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Thr Ala Ala Arg Glu Ser Met Pro Tyr Thr Asn Ala Val Ile His Glu
 355 360 365

Val Gln Arg Met Gly Asn Ile Ile Pro Leu Asn Val Pro Arg Glu Val
 370 375 380

Thr Val Asp Thr Thr Leu Ala Gly Tyr His Leu Pro Lys Gly Thr Met
 385 390 395 400

Ile Leu Thr Asn Leu Thr Ala Leu His Arg Asp Pro Thr Glu Trp Ala
 405 410 415

Thr Pro Asp Thr Phe Asn Pro Asp His Phe Leu Glu Asn Gly Gln Phe
 420 425 430

Lys Lys Arg Glu Ala Phe Met Pro Phe Ser Ile Gly Lys Arg Ala Cys
 435 440 445

Leu Gly Glu Gln Leu Ala Arg Thr Glu Leu Phe Ile Phe Phe Thr Ser
 450 455 460

Leu Met Gln Lys Phe Thr Phe Arg Pro Pro Asn Asn Glu Lys Leu Ser
 465 470 475 480

Leu Lys Phe Arg Met Gly Ile Thr Ile Ser Pro Val Ser His Arg Leu
 485 490 495

Cys Ala Val Pro Gln Val
 500

<210> 137
 <211> 766
 <212> PRT
 <213> Human

<400> 137

Met Lys Thr Pro Trp Arg Val Leu Leu Gly Leu Leu Gly Ala Ala Ala
 1 5 10 15

Leu Val Thr Ile Ile Thr Val Pro Val Val Leu Leu Asn Lys Gly Thr
 20 25 30

Asp Asp Ala Thr Ala Asp Ser Arg Lys Thr Tyr Thr Leu Thr Asp Tyr
 35 40 45

Leu Lys Asn Thr Tyr Arg Leu Lys Leu Tyr Ser Leu Arg Trp Ile Ser
50 55 60

Asp His Glu Tyr Leu Tyr Lys Gln Glu Asn Asn Ile Leu Val Phe Asn
65 70 75 80

Ala Glu Tyr Gly Asn Ser Ser Val Phe Leu Glu Asn Ser Thr Phe Asp
85 90 95

Glu Phe Gly His Ser Ile Asn Asp Tyr Ser Ile Ser Pro Asp Gly Gln
100 105 110

Phe Ile Leu Leu Glu Tyr Asn Tyr Val Lys Gln Trp Arg His Ser Tyr
115 120 125

Thr Ala Ser Tyr Asp Ile Tyr Asp Leu Asn Lys Arg Gln Leu Ile Thr
130 135 140

Glu Glu Arg Ile Pro Asn Asn Thr Gln Trp Val Thr Trp Ser Pro Val
145 150 155 160

Gly His Lys Leu Ala Tyr Val Trp Asn Asn Asp Ile Tyr Val Lys Ile
165 170 175

Glu Pro Asn Leu Pro Ser Tyr Arg Ile Thr Trp Thr Gly Lys Glu Asp
180 185 190

Ile Ile Tyr Asn Gly Ile Thr Asp Trp Val Tyr Glu Glu Glu Val Phe
195 200 205

Ser Ala Tyr Ser Ala Leu Trp Trp Ser Pro Asn Gly Thr Phe Leu Ala
210 215 220

Tyr Ala Gln Phe Asn Asp Thr Glu Val Pro Leu Ile Glu Tyr Ser Phe
225 230 235 240

Tyr Ser Asp Glu Ser Leu Gln Tyr Pro Lys Thr Val Arg Val Pro Tyr
245 250 255

Pro Lys Ala Gly Ala Val Asn Pro Thr Val Lys Phe Phe Val Val Asn
260 265 270

Thr Asp Ser Leu Ser Ser Val Thr Asn Ala Thr Ser Ile Gln Ile Thr
275 280 285

Ala Pro Ala Ser Met Leu Ile Gly Asp His Tyr Leu Cys Asp Val Thr
 290 295 300
 Trp Ala Thr Gln Glu Arg Ile Ser Leu Gln Trp Leu Arg Arg Ile Gln
 305 310 315 320
 Asn Tyr Ser Val Met Asp Ile Cys Asp Tyr Asp Glu Ser Ser Gly Arg
 325 330 335
 Trp Asn Cys Leu Val Ala Arg Gln His Ile Glu Met Ser Thr Thr Gly
 340 345 350
 Trp Val Gly Arg Phe Arg Pro Ser Glu Pro His Phe Thr Leu Asp Gly
 355 360 365
 Asn Ser Phe Tyr Lys Ile Ile Ser Asn Glu Glu Gly Tyr Arg His Ile
 370 375 380
 Cys Tyr Phe Gln Ile Asp Lys Lys Asp Cys Thr Phe Ile Thr Lys Gly
 385 390 395 400
 Thr Trp Glu Val Ile Gly Ile Glu Ala Leu Thr Ser Asp Tyr Leu Tyr
 405 410 415
 Tyr Ile Ser Asn Glu Tyr Lys Gly Met Pro Gly Gly Arg Asn Leu Tyr
 420 425 430
 Lys Ile Gln Leu Ser Asp Tyr Thr Lys Val Thr Cys Leu Ser Cys Glu
 435 440 445
 Leu Asn Pro Glu Arg Cys Gln Tyr Tyr Ser Val Ser Phe Ser Lys Glu
 450 455 460
 Ala Lys Tyr Tyr Gln Leu Arg Cys Ser Gly Pro Gly Leu Pro Leu Tyr
 465 470 475 480
 Thr Leu His Ser Ser Val Asn Asp Lys Gly Leu Arg Val Leu Glu Asp
 485 490 495
 Asn Ser Ala Leu Asp Lys Met Leu Gln Asn Val Gln Met Pro Ser Lys
 500 505 510
 Lys Leu Asp Phe Ile Ile Leu Asn Glu Thr Lys Phe Trp Tyr Gln Met
 515 520 525

Ile Leu Pro Pro His Phe Asp Lys Ser Lys Lys Tyr Pro Leu Leu Leu
 530 535 540

Asp Val Tyr Ala Gly Pro Cys Ser Gln Lys Ala Asp Ile Val Phe Arg
 545 550 555 560

Leu Asn Trp Ala Thr Tyr Leu Ala Ser Thr Glu Asn Ile Ile Val Ala
 565 570 575

Ser Phe Asp Gly Arg Gly Ser Gly Tyr Gln Gly Asp Lys Ile Met His
 580 585 590

Ala Ile Asn Arg Arg Leu Gly Thr Phe Glu Val Glu Asp Gln Ile Glu
 595 600 605

Ala Ala Arg Gln Phe Ser Lys Met Gly Phe Val Asp Asn Lys Arg Ile
 610 615 620

Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Thr Ser Met Val Leu
 625 630 635 640

Gly Ser Gly Ser Gly Val Phe Lys Cys Gly Ile Ala Val Ala Pro Val
 645 650 655

Ser Arg Trp Glu Tyr Tyr Glu Ser Val Tyr Thr Glu Arg Tyr Met Gly
 660 665 670

Leu Pro Thr Pro Glu Asp Asn Leu Asp His Tyr Arg Asn Ser Thr Val
 675 680 685

Met Ser Arg Ala Glu Asn Phe Lys Gln Val Glu Tyr Leu Leu Ile His
 690 695 700

Gly Thr Ala Asp Asp Asn Val His Phe Gln Gln Ser Ala Gln Ile Ser
 705 710 715 720

Lys Ala Leu Val Asp Val Gly Val Asp Phe Gln Ala Met Trp Tyr Thr
 725 730 735

Asp Glu Asp His Gly Ile Ala Ser Ser Thr Ala His Gln His Ile Tyr
 740 745 750

Thr His Met Ser His Phe Ile Lys Gln Cys Phe Ser Leu Pro

317/439

195	200	205
Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu		
210	215	220
Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg		
225	230	235 240
Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu		
	245	250 255
Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly		
	260	265 270
Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp		
	275	280 285
Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu		
290	295	300
Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala		
305	310	315 320
Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro		
	325	330 335
Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp		
	340	345 350
Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val		
355	360	365
Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln		
370	375	380
Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Ala Leu Thr		
385	390	395 400
Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr		
	405	410 415
Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly		
420	425	430

His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Glu Ser Leu
 435 440 445
 Ser Gly Leu Ser Leu Arg Leu Val Lys Lys Glu Pro Arg Gln Leu Glu
 450 455 460
 Leu Thr Trp Ala Gly Ser Arg Pro Arg Ser Pro Gly Ala Asn Leu Thr
 465 470 475 480
 Tyr Glu Leu His Val Leu Asn Gln Asp Glu Glu Arg Tyr Gln Met Val
 485 490 495
 Leu Glu Pro Arg Val Leu Leu Thr Glu Leu Gln Pro Asp Thr Thr Tyr
 500 505 510
 Ile Val Arg Val Arg Met Leu Thr Pro Leu Gly Pro Gly Pro Phe Ser
 515 520 525
 Pro Asp His Glu Phe Arg Thr Ser Pro Pro Val Ser Arg Gly Leu Thr
 530 535 540
 Gly Gly Glu Ile Val Ala Val Ile Phe Gly Leu Leu Leu Gly Ala Ala
 545 550 555 560
 Leu Leu Leu Gly Ile Leu Val Phe Arg Ser Arg Arg Ala Gln Arg Gln
 565 570 575
 Arg Gln Gln Arg His Val Thr Ala Pro Pro Met Trp Ile Glu Arg Thr
 580 585 590
 Ser Cys Ala Glu Ala Leu Cys Gly Thr Ser Arg His Thr Arg Thr Leu
 595 600 605
 His Arg Glu Pro Trp Thr Leu Pro Gly Gly Trp Ser Asn Phe Pro Ser
 610 615 620
 Arg Glu Leu Asp Pro Ala Trp Leu Met Val Asp Thr Val Ile Gly Glu
 625 630 635 640
 Gly Glu Phe Gly Glu Val Tyr Arg Gly Thr Leu Arg Leu Pro Ser Gln
 645 650 655
 Asp Cys Lys Thr Val Ala Ile Lys Thr Leu Lys Asp Thr Ser Pro Gly
 660 665 670

Gly Gln Trp Trp Asn Phe Leu Arg Glu Ala Thr Ile Met Gly Gln Phe
675 680 685

Ser His Pro His Ile Leu His Leu Glu Gly Val Val Thr Lys Arg Lys
690 695 700

Pro Ile Met Ile Ile Thr Glu Phe Met Glu Asn Ala Ala Leu Asp Ala
705 710 715 720

Phe Leu Arg Glu Arg Glu Asp Gln Leu Val Pro Gly Gln Leu Val Ala
725 730 735

Met Leu Gln Gly Ile Ala Ser Gly Met Asn Tyr Leu Ser Asn His Asn
740 745 750

Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Gln Asn
755 760 765

Leu Cys Cys Lys Val Ser Asp Phe Gly Leu Thr Arg Leu Leu Asp Asp
770 775 780

Phe Asp Gly Thr Tyr Glu Thr Gln Gly Gly Lys Ile Pro Ile Arg Trp
785 790 795 800

Thr Ala Pro Glu Ala Ile Ala His Arg Ile Phe Thr Thr Ala Ser Asp
805 810 815

Val Trp Ser Phe Gly Ile Val Met Trp Glu Val Leu Ser Phe Gly Asp
820 825 830

Lys Pro Tyr Gly Glu Met Ser Asn Gln Glu Val Met Lys Ser Ile Glu
835 840 845

Asp Gly Tyr Arg Leu Pro Pro Pro Val Asp Cys Pro Ala Pro Leu Tyr
850 855 860

Glu Leu Met Lys Asn Cys Trp Ala Tyr Asp Arg Ala Arg Arg Pro His
865 870 875 880

Phe Gln Lys Leu Gln Ala His Leu Glu Gln Leu Leu Ala Asn Pro His
885 890 895

Ser Leu Arg Thr Ile Ala Asn Phe Asp Pro Arg Val Thr Leu Arg Leu
900 905 910

Pro Ser Leu Ser Gly Ser Asp Gly Ile Pro Tyr Arg Thr Val Ser Glu
 915 920 925

Trp Leu Glu Ser Ile Arg Met Lys Arg Tyr Ile Leu His Phe His Ser
 930 935 940

Ala Gly Leu Asp Thr Met Glu Cys Val Leu Glu Leu Thr Ala Glu Asp
 945 950 955 960

Leu Thr Gln Met Gly Ile Thr Leu Pro Gly His Gln Lys Arg Ile Leu
 965 970 975

Cys Ser Ile Gln Gly Phe Lys Asp
 980

<210> 139
 <211> 822
 <212> PRT
 <213> Human

<400> 139

Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
 1 5 10 15

Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
 20 25 30

Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
 35 40 45

Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
 50 55 60

Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
 65 70 75 80

Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
 85 90 95

Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
 100 105 110

Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
 115 120 125

Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
 130 135 140

Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
 145 150 155 160

Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
 165 170 175

Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
 180 185 190

Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
 195 200 205

Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
 210 215 220

Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
 225 230 235 240

Asn His Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro
 245 250 255

Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly
 260 265 270

Asp Val Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
 275 280 285

Gln Trp Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
 290 295 300

Gly Leu Pro Tyr Leu Lys Val Leu Lys His Ser Gly Ile Asn Ser Ser
 305 310 315 320

Asn Ala Glu Val Leu Ala Leu Phe Asn Val Thr Glu Ala Asp Ala Gly
 325 330 335

Glu Tyr Ile Cys Lys Val Ser Asn Tyr Ile Gly Gln Ala Asn Gln Ser
 340 345 350

Ala Trp Leu Thr Val Leu Pro Lys Gln Gln Ala Pro Gly Arg Glu Lys

355	360	365
Glu Ile Thr Ala Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys Ile 370 375 380		
Gly Val Phe Leu Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg 385 390 395 400		
Met Lys Asn Thr Thr Lys Lys Pro Asp Phe Ser Ser Gln Pro Ala Val 405 410 415		
His Lys Leu Thr Lys Arg Ile Pro Leu Arg Arg Gln Val Thr Val Ser 420 425 430		
Ala Glu Ser Ser Ser Ser Met Asn Ser Asn Thr Pro Leu Val Arg Ile 435 440 445		
Thr Thr Arg Leu Ser Ser Thr Ala Asp Thr Pro Met Leu Ala Gly Val 450 455 460		
Ser Glu Tyr Glu Leu Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp 465 470 475 480		
Lys Leu Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val 485 490 495		
Val Met Ala Glu Ala Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala 500 505 510		
Val Thr Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp 515 520 525		
Leu Ser Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys 530 535 540		
His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro 545 550 555 560		
Leu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr 565 570 575		
Leu Arg Ala Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn 580 585 590		

Arg Val Pro Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr
 595 600 605

Tyr Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile
 610 615 620

His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val
 625 630 635 640

Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp
 645 650 655

Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala
 660 665 670

Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp
 675 680 685

Ser Phe Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro
 690 695 700

Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly
 705 710 715 720

His Arg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met
 725 730 735

Met Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys
 740 745 750

Gln Leu Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu
 755 760 765

Glu Tyr Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr
 770 775 780

Pro Asp Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser
 785 790 795 800

Pro Asp Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile
 805 810 815

Asn Gly Ser Val Lys Thr
 820

<210> 140
 <211> 87
 <212> PRT
 <213> Human

<400> 140

Met Gln Lys Val Thr Leu Gly Leu Leu Val Phe Leu Ala Gly Phe Pro
 1 5 10 15

Val Leu Asp Ala Asn Asp Leu Glu Asp Lys Asn Ser Pro Phe Tyr Tyr
 20 25 30

Asp Trp His Ser Leu Gln Val Gly Gly Leu Ile Cys Ala Gly Val Leu
 35 40 45

Cys Ala Met Gly Ile Ile Ile Val Met Ser Ala Lys Cys Lys Cys Lys
 50 55 60

Phe Gly Gln Lys Ser Gly His His Pro Gly Glu Thr Pro Pro Leu Ile
 65 70 75 80

Thr Pro Gly Ser Ala Gln Ser
 85

<210> 141
 <211> 907
 <212> PRT
 <213> Human

<400> 141

Met Asp Thr Ser Arg Leu Gly Val Leu Leu Ser Leu Pro Val Leu Leu
 1 5 10 15

Gln Leu Ala Thr Gly Gly Ser Ser Pro Arg Ser Gly Val Leu Leu Arg
 20 25 30

Gly Cys Pro Thr His Cys His Cys Glu Pro Asp Gly Arg Met Leu Leu
 35 40 45

Arg Val Asp Cys Ser Asp Leu Gly Leu Ser Glu Leu Pro Ser Asn Leu
 50 55 60

Ser Val Phe Thr Ser Tyr Leu Asp Leu Ser Met Asn Asn Ile Ser Gln
 65 70 75 80

Leu Leu Pro Asn Pro Leu Pro Ser Leu Arg Phe Leu Glu Glu Leu Arg
 85 90 95

Leu Ala Gly Asn Ala Leu Thr Tyr Ile Pro Lys Gly Ala Phe Thr Gly
 100 105 110

Leu Tyr Ser Leu Lys Val Leu Met Leu Gln Asn Asn Gln Leu Arg His
 115 120 125

Val Pro Thr Glu Ala Leu Gln Asn Leu Arg Ser Leu Gln Ser Leu Arg
 130 135 140

Leu Asp Ala Asn His Ile Ser Tyr Val Pro Pro Ser Cys Phe Ser Gly
 145 150 155 160

Leu His Ser Leu Arg His Leu Trp Leu Asp Asp Asn Ala Leu Thr Glu
 165 170 175

Ile Pro Val Gln Ala Phe Arg Ser Leu Ser Ala Leu Gln Ala Met Thr
 180 185 190

Leu Ala Leu Asn Lys Ile His His Ile Pro Asp Tyr Ala Phe Gly Asn
 195 200 205

Leu Ser Ser Leu Val Val Leu His Leu His Asn Asn Arg Ile His Ser
 210 215 220

Leu Gly Lys Lys Cys Phe Asp Gly Leu His Ser Leu Glu Thr Leu Asp
 225 230 235 240

Leu Asn Tyr Asn Asn Leu Asp Glu Phe Pro Thr Ala Ile Arg Thr Leu
 245 250 255

Ser Asn Leu Lys Glu Leu Gly Phe His Ser Asn Asn Ile Arg Ser Ile
 260 265 270

Pro Glu Lys Ala Phe Val Gly Asn Pro Ser Leu Ile Thr Ile His Phe
 275 280 285

Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser Ala Phe Gln His Leu
 290 295 300

Pro Glu Leu Arg Thr Leu Thr Leu Asn Gly Ala Ser Gln Ile Thr Glu
 305 310 315 320

Phe Pro Asp Leu Thr Gly Thr Ala Asn Leu Glu Ser Leu Thr Leu Thr
 325 330 335
 Gly Ala Gln Ile Ser Ser Leu Pro Gln Thr Val Cys Asn Gln Leu Pro
 340 345 350
 Asn Leu Gln Val Leu Asp Leu Ser Tyr Asn Leu Leu Glu Asp Leu Pro
 355 360 365
 Ser Phe Ser Val Cys Gln Lys Leu Gln Lys Ile Asp Leu Arg His Asn
 370 375 380
 Glu Ile Tyr Glu Ile Lys Val Asp Thr Phe Gln Gln Leu Leu Ser Leu
 385 390 395 400
 Arg Ser Leu Asn Leu Ala Trp Asn Lys Ile Ala Ile Ile His Pro Asn
 405 410 415
 Ala Phe Ser Thr Leu Pro Ser Leu Ile Lys Leu Asp Leu Ser Ser Asn
 420 425 430
 Leu Leu Ser Ser Phe Pro Ile Thr Gly Leu His Gly Leu Thr His Leu
 435 440 445
 Lys Leu Thr Gly Asn His Ala Leu Gln Ser Leu Ile Ser Ser Glu Asn
 450 455 460
 Phe Pro Glu Leu Lys Val Ile Glu Met Pro Tyr Ala Tyr Gln Cys Cys
 465 470 475 480
 Ala Phe Gly Val Cys Glu Asn Ala Tyr Lys Ile Ser Asn Gln Trp Asn
 485 490 495
 Lys Gly Asp Asn Ser Ser Met Asp Asp Leu His Lys Lys Asp Ala Gly
 500 505 510
 Met Phe Gln Ala Gln Asp Glu Arg Asp Leu Glu Asp Phe Leu Leu Asp
 515 520 525
 Phe Glu Glu Asp Leu Lys Ala Leu His Ser Val Gln Cys Ser Pro Ser
 530 535 540
 Pro Gly Pro Phe Lys Pro Cys Glu His Leu Leu Asp Gly Trp Leu Ile
 545 550 555 560

Arg Ile Gly Val Trp Thr Ile Ala Val Leu Ala Leu Thr Cys Asn Ala
565 570 575

Leu Val Thr Ser Thr Val Phe Arg Ser Pro Leu Tyr Ile Ser Pro Ile
580 585 590

Lys Leu Leu Ile Gly Val Ile Ala Ala Val Asn Met Leu Thr Gly Val
595 600 605

Ser Ser Ala Val Leu Ala Gly Val Asp Ala Phe Thr Phe Gly Ser Phe
610 615 620

Ala Arg His Gly Ala Trp Trp Glu Asn Gly Val Gly Cys His Val Ile
625 630 635 640

Gly Phe Leu Ser Ile Phe Ala Ser Glu Ser Ser Val Phe Leu Leu Thr
645 650 655

Leu Ala Ala Leu Glu Arg Gly Phe Ser Val Lys Tyr Ser Ala Lys Phe
660 665 670

Glu Thr Lys Ala Pro Phe Ser Ser Leu Lys Val Ile Ile Leu Leu Cys
675 680 685

Ala Leu Leu Ala Leu Thr Met Ala Ala Val Pro Leu Leu Gly Gly Ser
690 695 700

Lys Tyr Gly Ala Ser Pro Leu Cys Leu Pro Leu Pro Phe Gly Glu Pro
705 710 715 720

Ser Thr Met Gly Tyr Met Val Ala Leu Ile Leu Leu Asn Ser Leu Cys
725 730 735

Phe Leu Met Met Thr Ile Ala Tyr Thr Lys Leu Tyr Cys Asn Leu Asp
740 745 750

Lys Gly Asp Leu Glu Asn Ile Trp Asp Cys Ser Met Val Lys His Ile
755 760 765

Ala Leu Leu Leu Phe Thr Asn Cys Ile Leu Asn Cys Pro Val Ala Phe
770 775 780

Leu Ser Phe Ser Ser Leu Ile Asn Leu Thr Phe Ile Ser Pro Glu Val

785 790 795 800

Ile Lys Phe Ile Leu Leu Val Val Val Pro Leu Pro Ala Cys Leu Asn
805 810 815

Pro Leu Leu Tyr Ile Leu Phe Asn Pro His Phe Lys Glu Asp Leu Val
820 825 830

Ser Leu Arg Lys Gln Thr Tyr Val Trp Thr Arg Ser Lys His Pro Ser
835 840 845

Leu Met Ser Ile Asn Ser Asp Asp Val Glu Lys Gln Ser Cys Asp Ser
850 855 860

Thr Gln Ala Leu Val Thr Phe Thr Ser Ser Ser Ile Thr Tyr Asp Leu
865 870 875 880

Pro Pro Ser Ser Val Pro Ser Pro Ala Tyr Pro Val Thr Glu Ser Cys
885 890 895

His Leu Ser Ser Val Ala Phe Val Pro Cys Leu
900 905

<210> 142
<211> 1134
<212> PRT
<213> Human

<400> 142

Met Glu Ser Thr Pro Ser Phe Leu Lys Gly Thr Pro Thr Trp Glu Lys
1 5 10 15

Thr Ala Pro Glu Asn Gly Ile Val Arg Gln Glu Pro Gly Ser Pro Pro
20 25 30

Arg Asp Gly Leu His His Gly Pro Leu Cys Leu Gly Glu Pro Ala Pro
35 40 45

Phe Trp Arg Gly Val Leu Ser Thr Pro Asp Ser Trp Leu Pro Pro Gly
50 55 60

Phe Pro Gln Gly Pro Lys Asp Met Leu Pro Leu Val Glu Gly Glu Gly
65 70 75 80

Pro Gln Asn Gly Glu Arg Lys Val Asn Trp Leu Gly Ser Lys Glu Gly

85	90	95
Leu Arg Trp Lys Glu Ala Met Leu Thr His Pro Leu Ala Phe Cys Gly		
100	105	110
Pro Ala Cys Pro Pro Arg Cys Gly Pro Leu Met Pro Glu His Ser Gly		
115	120	125
Gly His Leu Lys Ser Asp Pro Val Ala Phe Arg Pro Trp His Cys Pro		
130	135	140
Phe Leu Leu Glu Thr Lys Ile Leu Glu Arg Ala Pro Phe Trp Val Pro		
145	150	155
Thr Cys Leu Pro Pro Tyr Leu Val Ser Gly Leu Pro Pro Glu His Pro		
165	170	175
Cys Asp Trp Pro Leu Thr Pro His Pro Trp Val Tyr Ser Gly Gly Gln		
180	185	190
Pro Lys Val Pro Ser Ala Phe Ser Leu Gly Ser Lys Gly Phe Tyr Tyr		
195	200	205
Lys Asp Pro Ser Ile Pro Arg Leu Ala Lys Glu Pro Leu Ala Ala Ala		
210	215	220
Glu Pro Gly Leu Phe Gly Leu Asn Ser Gly Gly His Leu Gln Arg Ala		
225	230	235
Gly Glu Ala Glu Arg Pro Ser Leu His Gln Arg Asp Gly Glu Met Gly		
245	250	255
Ala Gly Arg Gln Gln Asn Pro Cys Pro Leu Phe Leu Gly Gln Pro Asp		
260	265	270
Thr Val Pro Trp Thr Ser Trp Pro Ala Cys Pro Pro Gly Leu Val His		
275	280	285
Thr Leu Gly Asn Val Trp Ala Gly Pro Gly Asp Gly Asn Leu Gly Tyr		
290	295	300
Gln Leu Gly Pro Pro Ala Thr Pro Arg Cys Pro Ser Pro Glu Pro Pro		
305	310	315
		320

Val Thr Gln Arg Gly Cys Cys Ser Ser Tyr Pro Pro Thr Lys Gly Gly
 325 330 335

Gly Leu Gly Pro Cys Gly Lys Cys Gln Glu Gly Leu Glu Gly Gly Ala
 340 345 350

Ser Gly Ala Ser Glu Pro Ser Glu Glu Val Asn Lys Ala Ser Gly Pro
 355 360 365

Arg Ala Cys Pro Pro Ser His His Thr Lys Leu Lys Lys Thr Trp Leu
 370 375 380

Thr Arg His Ser Glu Gln Phe Glu Cys Pro Arg Gly Cys Pro Glu Val
 385 390 395 400

Glu Glu Arg Pro Val Ala Arg Leu Arg Ala Leu Lys Arg Ala Gly Ser
 405 410 415

Pro Glu Val Gln Gly Ala Met Gly Ser Pro Ala Pro Lys Arg Pro Pro
 420 425 430

Asp Pro Phe Pro Gly Thr Ala Glu Gln Gly Ala Gly Gly Trp Gln Glu
 435 440 445

Val Arg Asp Thr Ser Ile Gly Asn Lys Asp Val Asp Ser Gly Gln His
 450 455 460

Asp Glu Gln Lys Gly Pro Gln Asp Gly Gln Ala Ser Leu Gln Asp Pro
 465 470 475 480

Gly Leu Gln Asp Ile Pro Cys Leu Ala Leu Pro Ala Lys Leu Ala Gln
 485 490 495

Cys Gln Ser Cys Ala Gln Ala Ala Gly Glu Gly Gly Gly His Ala Cys
 500 505 510

His Ser Gln Gln Val Arg Arg Ser Pro Leu Gly Gly Glu Leu Gln Gln
 515 520 525

Glu Glu Asp Thr Ala Thr Asn Ser Ser Ser Glu Glu Gly Pro Gly Ser
 530 535 540

Gly Pro Asp Ser Arg Leu Ser Thr Gly Leu Ala Lys His Leu Leu Ser
 545 550 555 560

Gly Leu Gly Asp Arg Leu Cys Arg Leu Leu Arg Arg Glu Arg Glu Ala
 565 570 575

Leu Ala Trp Ala Gln Arg Glu Gly Gln Gly Pro Ala Val Thr Glu Asp
 580 585 590

Ser Pro Gly Ile Pro Arg Cys Cys Ser Arg Cys His His Gly Leu Phe
 595 600 605

Asn Thr His Trp Arg Cys Pro Arg Cys Ser His Arg Leu Cys Val Ala
 610 615 620

Cys Gly Arg Val Ala Gly Thr Gly Arg Ala Arg Glu Lys Ala Gly Phe
 625 630 635 640

Gln Glu Gln Ser Ala Glu Glu Cys Thr Gln Glu Ala Gly His Ala Ala
 645 650 655

Cys Ser Leu Met Leu Thr Gln Phe Val Ser Ser Gln Ala Leu Ala Glu
 660 665 670

Leu Ser Thr Ala Met His Gln Val Trp Val Lys Phe Asp Ile Arg Gly
 675 680 685

His Cys Pro Cys Gln Ala Asp Ala Arg Val Trp Ala Pro Gly Asp Ala
 690 695 700

Gly Gln Gln Lys Glu Ser Thr Gln Lys Thr Pro Pro Thr Pro Gln Pro
 705 710 715 720

Ser Cys Asn Gly Asp Thr His Arg Thr Lys Ser Ile Lys Glu Glu Thr
 725 730 735

Pro Asp Ser Ala Glu Thr Pro Ala Glu Asp Arg Ala Gly Arg Gly Pro
 740 745 750

Leu Pro Cys Pro Ser Leu Cys Glu Leu Leu Ala Ser Thr Ala Val Lys
 755 760 765

Leu Cys Leu Gly His Glu Arg Ile His Met Ala Phe Ala Pro Val Thr
 770 775 780

Pro Ala Leu Pro Ser Asp Asp Arg Ile Thr Asn Ile Leu Asp Ser Ile
 785 790 795 800

Ile Ala Gln Val Val Glu Arg Lys Ile Gln Glu Lys Ala Leu Gly Pro
 805 810 815

Gly Leu Arg Ala Gly Pro Gly Leu Arg Lys Gly Leu Gly Leu Pro Leu
 820 825 830

Ser Pro Val Arg Pro Arg Leu Pro Pro Pro Gly Ala Leu Leu Trp Leu
 835 840 845

Gln Glu Pro Gln Pro Cys Pro Arg Arg Gly Phe His Leu Phe Gln Glu
 850 855 860

His Trp Arg Gln Gly Gln Pro Val Leu Val Ser Gly Ile Gln Arg Thr
 865 870 875 880

Leu Gln Gly Asn Leu Trp Gly Thr Glu Ala Leu Gly Ala Leu Gly Gly
 885 890 895

Gln Val Gln Ala Leu Ser Pro Leu Gly Pro Pro Gln Pro Ser Ser Leu
 900 905 910

Gly Ser Thr Thr Phe Trp Glu Gly Phe Ser Trp Pro Glu Leu Arg Pro
 915 920 925

Lys Ser Asp Glu Gly Ser Val Leu Leu Leu His Arg Ala Leu Gly Asp
 930 935 940

Glu Asp Thr Ser Arg Val Glu Asn Leu Ala Ala Ser Leu Pro Leu Pro
 945 950 955 960

Glu Tyr Cys Ala Leu His Gly Lys Leu Asn Leu Ala Ser Tyr Leu Pro
 965 970 975

Pro Gly Leu Ala Leu Arg Pro Leu Glu Pro Gln Leu Trp Ala Ala Tyr
 980 985 990

Gly Val Ser Pro His Arg Gly His Leu Gly Thr Lys Asn Leu Cys Val
 995 1000 1005

Glu Val Ala Asp Leu Val Ser Ile Leu Val His Ala Asp Thr Pro
 1010 1015 1020

Leu Pro Ala Trp His Arg Ala Gln Lys Asp Phe Leu Ser Gly Leu

1025 1030 1035
 Asp Gly Glu Gly Leu Trp Ser Pro Gly Ser Gln Val Ser Thr Val
 1040 1045 1050
 Trp His Val Phe Arg Ala Gln Asp Ala Gln Arg Ile Arg Arg Phe
 1055 1060 1065
 Leu Gln Met Val Gln Gly Leu Val Ser Thr Val Ser Val Thr Gln
 1070 1075 1080
 His Phe Leu Ser Pro Glu Thr Ser Ala Leu Ser Ala Gln Leu Cys
 1085 1090 1095
 His Gln Gly Pro Ser Leu Pro Pro Asp Cys His Leu Leu Tyr Ala
 1100 1105 1110
 Gln Met Asp Trp Ala Val Phe Gln Ala Val Lys Val Ala Val Gly
 1115 1120 1125
 Thr Leu Gln Glu Ala Lys
 1130
 <210> 143
 <211> 142
 <212> PRT
 <213> Human
 <400> 143
 Met Val Leu Ser Pro Ala Asp Lys Thr Asn Val Lys Ala Ala Trp Gly
 1 5 10 15
 Lys Val Gly Ala His Ala Gly Glu Tyr Gly Ala Glu Ala Leu Glu Arg
 20 25 30
 Met Phe Leu Ser Phe Pro Thr Thr Lys Thr Tyr Phe Pro His Phe Asp
 35 40 45
 Leu Ser His Gly Ser Ala Gln Val Lys Gly His Gly Lys Lys Val Ala
 50 55 60
 Asp Ala Leu Thr Asn Ala Val Ala His Val Asp Asp Met Pro Asn Ala
 65 70 75 80
 Leu Ser Ala Leu Ser Asp Leu His Ala His Lys Leu Arg Val Asp Pro

335/439

145 150 155 160
 Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
 165 170 175
 Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
 180 185 190
 Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
 195 200 205
 Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
 210 215 220
 Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
 225 230 235 240
 Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser
 245 250 255
 Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
 260 265 270
 Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
 275 280 285
 Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
 290 295 300
 Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
 305 310 315 320
 Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
 325 330 335
 Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala
 340 345 350
 Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
 355 360 365
 Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
 370 375 380

Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
385 390 395 400

Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
405 410 415

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
420 425 430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
435 440 445

Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
450 455 460

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
465 470 475 480

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
485 490 495

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
500 505 510

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
515 520' 525

Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
530 535 540

<210> 145
<211> 203
<212> PRT
<213> Human

<400> 145

Cys Ser Val Pro Phe Leu Pro Leu Ala Val Pro Val Arg Ala Val His
1 5 10 15

Arg Leu Leu Glu His Arg His His Ser Val Thr Trp Pro Ala Thr Glu
20 25 30

Leu Pro Ile Thr Gln Leu Thr Ser Ser Ile Val Arg Arg Val Asn Glu
35 40 45

Ala Ser Gly Leu Tyr Gln Met Phe Gly Val Leu Ala Asp Val Ile Leu
50 55 60

Leu Lys Glu Thr Gly Gly Glu Val Pro Pro Cys Thr Leu Ala Pro Ala
65 70 75 80

Ser Ala His Gly His Pro Ser His Arg Gly Arg Leu Leu Asn Arg Leu
85 90 95

Asp Cys Pro Asp Arg Ala His Pro Thr Ser Glu Ala Leu Pro Gly Glu
100 105 110

Leu Phe Gly His Arg Phe Ala Lys Leu Leu Cys Arg Val Leu Leu Pro
115 120 125

Val Arg Pro His Ala Pro Glu Val Ala Thr Leu Leu Pro Ala Gly Val
130 135 140

Pro Glu Asp Ala Gly Thr Arg Glu Tyr Arg Glu Pro Leu Ala Ala Gln
145 150 155 160

Ser Gly Glu Gln Ala Pro Ala Gly Leu Cys Pro His Arg Gln Ala Pro
165 170 175

Gly Gly Gln Gln Pro Ala Ala Trp Arg Pro Arg Ala Thr Arg Phe Pro
180 185 190

Pro Gly Ser Arg Ala Ser Gly Ser Val Arg Arg
195 200

<210> 146

<211> 414

<212> PRT

<213> Human

<400> 146

Met Lys Ala Gln Thr Ala Leu Ser Phe Phe Leu Ile Leu Ile Thr Ser
1 5 10 15

Leu Ser Gly Ser Gln Gly Ile Phe Pro Leu Ala Phe Phe Ile Tyr Val
20 25 30

Pro Met Asn Glu Gln Ile Val Ile Gly Arg Leu Asp Glu Asp Ile Ile
35 40 45

Leu Pro Ser Ser Phe Glu Arg Gly Ser Glu Val Val Ile His Trp Lys
 50 55 60

Tyr Gln Asp Ser Tyr Lys Val His Ser Tyr Tyr Lys Gly Ser Asp His
 65 70 75 80

Leu Glu Ser Gln Asp Pro Arg Tyr Ala Asn Arg Thr Ser Leu Phe Tyr
 85 90 95

Asn Glu Ile Gln Asn Gly Asn Ala Ser Leu Phe Phe Arg Arg Val Ser
 100 105 110

Leu Leu Asp Glu Gly Ile Tyr Thr Cys Tyr Val Gly Thr Ala Ile Gln
 115 120 125

Val Ile Thr Asn Lys Val Val Leu Lys Val Gly Val Phe Leu Thr Pro
 130 135 140

Val Met Lys Tyr Glu Lys Arg Asn Thr Asn Ser Phe Leu Ile Cys Ser
 145 150 155 160

Val Leu Ser Val Tyr Pro Arg Pro Ile Ile Thr Trp Lys Met Asp Asn
 165 170 175

Thr Pro Ile Ser Glu Asn Asn Met Glu Glu Thr Gly Ser Leu Asp Ser
 180 185 190

Phe Ser Ile Asn Ser Pro Leu Asn Ile Thr Gly Ser Asn Ser Ser Tyr
 195 200 205

Glu Cys Thr Ile Glu Asn Ser Leu Leu Lys Gln Thr Trp Thr Gly Arg
 210 215 220

Trp Thr Met Lys Asp Gly Leu His Lys Met Gln Ser Glu His Val Ser
 225 230 235 240

Leu Ser Cys Gln Pro Val Asn Asp Tyr Phe Ser Pro Asn Gln Asp Phe
 245 250 255

Lys Val Thr Trp Ser Arg Met Lys Ser Gly Thr Phe Ser Val Leu Ala
 260 265 270

Tyr Tyr Leu Ser Ser Ser Gln Asn Thr Ile Ile Asn Glu Ser Arg Phe
 275 280 285

Ser Trp Asn Lys Glu Leu Ile Asn Gln Ser Asp Phe Ser Met Asn Leu
 290 295 300

Met Asp Leu Asn Leu Ser Asp Ser Gly Glu Tyr Leu Cys Asn Ile Ser
 305 310 315 320

Ser Asp Glu Tyr Thr Leu Leu Thr Ile His Thr Val His Val Glu Pro
 325 330 335

Ser Gln Glu Thr Ala Ser His Asn Lys Gly Leu Trp Ile Leu Val Pro
 340 345 350

Ser Ala Ile Leu Ala Ala Phe Leu Leu Ile Trp Ser Val Lys Cys Cys
 355 360 365

Arg Ala Gln Leu Glu Ala Arg Arg Ser Arg His Pro Ala Asp Gly Ala
 370 375 380

Gln Gln Glu Arg Cys Cys Val Pro Pro Gly Glu Arg Cys Pro Ser Ala
 385 390 395 400

Pro Asp Asn Gly Glu Glu Asn Val Pro Leu Ser Gly Lys Val
 405 410

<210> 147
 <211> 545
 <212> PRT
 <213> Human

<400> 147

Met Val Asp Ala Ala Glu Asn Leu Cys Pro Asn Val Met Lys Lys Ala
 1 5 10 15

His Ile Arg Gln Asp Leu Ile His Ala Ser Thr Glu Lys Ile Ser Ile
 20 25 30

Pro Arg Thr Phe Val Lys Asn Val Leu Leu Glu Gln Ser Gly Ile Asp
 35 40 45

Ile Leu Asn Lys Ile Ser Glu Val Lys Leu Thr Val Ala Ser Phe Leu
 50 55 60

Ser Asp Arg Ile Val Asp Glu Ile Leu Asp Ala Leu Ser His Cys His
 65 70 75 80

His Lys Leu Ala Asp His Phe Ser Arg Arg Gly Lys Thr Leu Pro Gln
 85 90 95

Gln Glu Ser Leu Glu Ile Glu Leu Ala Glu Glu Arg Pro Val Lys Arg
 100 105 110

Ser Ile Ile Thr Val Glu Glu Leu Thr Glu Ile Glu Arg Leu Glu Asp
 115 120 125

Leu Asp Thr Cys Met Met Thr Pro Lys Ser Lys Arg Lys Ser Ile His
 130 135 140

Ser Arg Met Leu Arg Pro Val Ser Arg Ala Phe Glu Met Glu Phe Asp
 145 150 155 160

Leu Asp Lys Ala Leu Glu Glu Val Pro Ile His Ile Glu Asp Pro Pro
 165 170 175

Phe Pro Ser Leu Arg Gln Glu Lys Arg Ser Ser Gly Phe Ile Ser Glu
 180 185 190

Leu Pro Ser Glu Glu Gly Lys Lys Leu Glu His Phe Thr Lys Leu Arg
 195 200 205

Pro Lys Arg Asn Lys Lys Gln Gln Pro Thr Gln Ala Ala Val Cys Ala
 210 215 220

Ala Asn Ile Val Ser Gln Asp Gly Glu Gln Asn Gly Leu Met Gly Arg
 225 230 235 240

Val Asp Glu Gly Val Asp Glu Phe Phe Thr Lys Lys Val Thr Lys Met
 245 250 255

Asp Ser Lys Lys Trp Ser Thr Arg Gly Ser Glu Ser His Glu Leu Asn
 260 265 270

Glu Gly Gly Asp Glu Lys Lys Lys Arg Asp Ser Arg Lys Ser Ser Gly
 275 280 285

Phe Leu Asn Leu Ile Lys Ser Arg Ser Lys Ser Glu Arg Pro Pro Thr
 290 295 300

Ile Leu Met Thr Glu Glu Pro Ser Ser Pro Lys Gly Ala Val Arg Ser
 305 310 315 320

Pro Pro Val Asp Cys Pro Arg Lys Asp Thr Lys Ala Ala Glu His Asn
325 330 335

Gly Asn Ser Glu Arg Ile Glu Glu Ile Lys Thr Pro Asp Ser Phe Glu
340 345 350

Glu Ser Gln Gly Glu Glu Ile Gly Lys Val Glu Arg Ser Asp Ser Lys
355 360 365

Ser Ser Pro Gln Ala Gly Arg Arg Tyr Gly Val Gln Val Met Gly Ser
370 375 380

Gly Leu Leu Ala Glu Met Lys Ala Lys Gln Glu Asn Arg Phe Gly Leu
385 390 395 400

Gly Thr Pro Glu Lys Asn Thr Lys Ala Glu Pro Lys Ala Glu Ala Gly
405 410 415

Ser Arg Ser Arg Ser Ser Ser Ser Thr Pro Thr Ser Pro Lys Pro Leu
420 425 430

Leu Gln Ser Pro Lys Pro Ser Leu Ala Ala Arg Pro Val Ile Pro Gln
435 440 445

Lys Pro Arg Thr Ala Ser Arg Pro Asp Asp Ile Pro Asp Ser Pro Ser
450 455 460

Ser Pro Lys Val Ala Leu Leu Pro Pro Val Leu Lys Lys Val Pro Ser
465 470 475 480

Asp Lys Glu Arg Asp Gly Gln Ser Ser Pro Gln Pro Ser Pro Arg Thr
485 490 495

Phe Ser Gln Glu Val Ser Arg Arg Ser Trp Gly Gln Gln Ala Gln Glu
500 505 510

Tyr Gln Glu Gln Lys Gln Arg Ser Ser Ser Lys Asp Gly His Gln Gly
515 520 525

Ser Lys Ser Asn Asp Ser Gly Glu Glu Ala Glu Lys Glu Phe Ile Phe
530 535 540

Val

545

<210> 148
 <211> 315
 <212> PRT
 <213> Human

<400> 148

Met Pro Leu Lys Leu Arg Gly Lys Lys Lys Ala Lys Ser Lys Glu Thr
 1 5 10 15

Ala Gly Leu Val Glu Gly Glu Pro Thr Gly Ala Gly Gly Gly Ser Leu
 20 25 30

Ser Ala Ser Arg Ala Pro Ala Arg Arg Leu Val Phe His Ala Gln Leu
 35 40 45

Ala His Gly Ser Ala Thr Gly Arg Val Glu Gly Phe Ser Ser Ile Gln
 50 55 60

Glu Leu Tyr Ala Gln Ile Ala Gly Ala Phe Glu Ile Ser Pro Ser Glu
 65 70 75 80

Ile Leu Tyr Cys Thr Leu Asn Thr Pro Lys Ile Asp Met Glu Arg Leu
 85 90 95

Leu Gly Gly Gln Leu Gly Leu Glu Asp Phe Ile Phe Ala His Val Lys
 100 105 110

Gly Ile Glu Lys Glu Val Asn Val Tyr Lys Ser Glu Asp Ser Leu Gly
 115 120 125

Leu Thr Ile Thr Asp Asn Gly Val Gly Tyr Ala Phe Ile Lys Arg Ile
 130 135 140

Lys Asp Gly Gly Val Ile Asp Ser Val Lys Thr Ile Cys Val Gly Asp
 145 150 155 160

His Ile Glu Ser Ile Asn Gly Glu Asn Ile Val Gly Trp Arg His Tyr
 165 170 175

Asp Val Ala Lys Lys Leu Lys Glu Leu Lys Lys Glu Glu Leu Phe Thr
 180 185 190

Met Lys Leu Ile Glu Pro Lys Lys Ala Phe Glu Ile Glu Leu Arg Ser

195 200 205
 Lys Ala Gly Lys Ser Ser Gly Glu Lys Ile Gly Cys Gly Arg Ala Thr
 210 215 220
 Leu Arg Leu Arg Ser Lys Gly Pro Ala Thr Val Glu Glu Met Pro Ser
 225 230 235 240
 Glu Thr Lys Ala Lys Ala Ile Glu Lys Ile Asp Asp Val Leu Glu Leu
 245 250 255
 Tyr Met Gly Ile Arg Asp Ile Asp Leu Ala Thr Thr Met Phe Glu Ala
 260 265 270
 Gly Lys Asp Lys Val Asn Pro Asp Glu Phe Ala Val Ala Leu Asp Glu
 275 280 285
 Thr Leu Gly Asp Phe Ala Phe Pro Asp Glu Phe Val Phe Asp Val Trp
 290 295 300
 Gly Val Ile Gly Asp Ala Lys Arg Arg Gly Leu
 305 310 315

 <210> 149
 <211> 486
 <212> PRT
 <213> Human

 <400> 149
 Met Pro Arg Pro Ala Pro Ala Arg Arg Leu Pro Gly Leu Leu Leu Leu
 1 5 10 15
 Leu Trp Pro Leu Leu Leu Leu Pro Ser Ala Ala Pro Asp Pro Val Ala
 20 25 30
 Arg Pro Gly Phe Arg Arg Leu Glu Thr Arg Gly Pro Gly Gly Ser Pro
 35 40 45
 Gly Arg Arg Pro Ser Pro Ala Ala Pro Asp Gly Ala Pro Ala Ser Gly
 50 55 60
 Thr Ser Glu Pro Gly Arg Ala Arg Gly Ala Gly Val Cys Lys Ser Arg
 65 70 75 80
 Pro Leu Asp Leu Val Phe Ile Ile Asp Ser Ser Arg Ser Val Arg Pro

85	90	95
Leu Glu Phe Thr Lys Val Lys Thr Phe Val Ser Arg Ile Ile Asp Thr		
100	105	110
Leu Asp Ile Gly Pro Ala Asp Thr Arg Val Ala Val Val Asn Tyr Ala		
115	120	125
Ser Thr Val Lys Ile Glu Phe Gln Leu Gln Ala Tyr Thr Asp Lys Gln		
130	135	140
Ser Leu Lys Gln Ala Val Gly Arg Ile Thr Pro Leu Ser Thr Gly Thr		
145	150	155
Met Ser Gly Leu Ala Ile Gln Thr Ala Met Asp Glu Ala Phe Thr Val		
165	170	175
Glu Ala Gly Ala Arg Glu Pro Ser Ser Asn Ile Pro Lys Val Ala Ile		
180	185	190
Ile Val Thr Asp Gly Arg Pro Gln Asp Gln Val Asn Glu Val Ala Ala		
195	200	205
Arg Ala Gln Ala Ser Gly Ile Glu Leu Tyr Ala Val Gly Val Asp Arg		
210	215	220
Ala Asp Met Ala Ser Leu Lys Met Met Ala Ser Glu Pro Leu Glu Glu		
225	230	235
His Val Phe Tyr Val Glu Thr Tyr Gly Val Ile Glu Lys Leu Ser Ser		
245	250	255
Arg Phe Gln Glu Thr Phe Cys Ala Leu Asp Pro Cys Val Leu Gly Thr		
260	265	270
His Gln Cys Gln His Val Cys Ile Ser Asp Gly Glu Gly Lys His His		
275	280	285
Cys Glu Cys Ser Gln Gly Tyr Thr Leu Asn Ala Asp Lys Lys Thr Cys		
290	295	300
Ser Ala Leu Asp Arg Cys Ala Leu Asn Thr His Gly Cys Glu His Ile		
305	310	315
		320

Cys Val Asn Asp Arg Ser Gly Ser Tyr His Cys Glu Cys Tyr Glu Gly
 325 330 335

Tyr Thr Leu Asn Glu Asp Arg Lys Thr Cys Ser Ala Gln Asp Lys Cys
 340 345 350

Ala Leu Gly Thr His Gly Cys Gln His Ile Cys Val Asn Asp Arg Thr
 355 360 365

Gly Ser His His Cys Glu Cys Tyr Glu Gly Tyr Thr Leu Asn Ala Asp
 370 375 380

Lys Lys Thr Cys Ser Val Arg Asp Lys Cys Ala Leu Gly Ser His Gly
 385 390 395 400

Cys Gln His Ile Cys Val Ser Asp Gly Ala Ala Ser Tyr His Cys Asp
 405 410 415

Cys Tyr Pro Gly Tyr Thr Leu Asn Glu Asp Lys Lys Thr Cys Ser Ala
 420 425 430

Thr Glu Glu Ala Arg Arg Leu Val Ser Thr Glu Asp Ala Cys Gly Cys
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Glu Ala Thr Leu Ala Phe Gln Asp Lys Val Ser Ser Tyr Leu Gln Arg
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Tyr Gly Gln Ile His Arg
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Arg Asp Ile Ser Ser Ser Leu Asn Ser Leu Ala Asp Ser Asn Ala Arg
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Glu Phe Glu Glu Glu Ser Lys Gln Pro Gly Val Ser Glu Gln Gln Arg
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His Gln Leu Lys His Arg Glu Leu Phe Leu Ser Arg Gln Phe Glu Ser
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Leu Pro Ala Thr His Ile Arg Gly Lys Cys Ser Val Thr Leu Leu Asn
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Glu Thr Asp Ile Leu Ser Gln Tyr Leu Glu Lys Glu Asp Cys Phe Phe
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Tyr Ser Leu Val Phe Asp Pro Val Gln Lys Thr Leu Leu Ala Asp Gln
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Gly Glu Ile Arg Val Gly Cys Lys Tyr Gln Ala Glu Ile Pro Asp Arg
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Leu Val Glu Gly Glu Ser Asp Asn Arg Asn Gln Gln Lys Met Glu Met
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Lys Val Trp Asp Pro Asp Asn Pro Leu Thr Asp Arg Gln Ile Asp Gln
 180 185 190

Phe Leu Val Val Ala Arg Ala Val Gly Thr Phe Ala Arg Ala Leu Asp
 195 200 205

Cys Ser Ser Ser Ile Arg Gln Pro Ser Leu His Met Ser Ala Ala Ala
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Ala Ser Arg Asp Ile Thr Leu Phe His Ala Met Asp Thr Leu Gln Arg
 225 230 235 240

Asn Gly Tyr Asp Leu Ala Lys Ala Met Ser Thr Leu Val Pro Gln Gly
 245 250 255

Gly Pro Val Leu Cys Arg Asp Glu Met Glu Glu Trp Ser Ala Ser Glu
 260 265 270

Ala Met Leu Phe Glu Glu Ala Leu Glu Lys Tyr Gly Lys Asp Phe Asn
 275 280 285

Asp Ile Arg Gln Asp Phe Leu Pro Trp Lys Ser Leu Ala Ser Ile Val
 290 295 300

Gln Phe Tyr Tyr Met Trp Lys Thr Thr Asp Arg Tyr Ile Gln Gln Lys
 305 310 315 320

Arg Leu Lys Ala Ala Glu Ala Asp Ser Lys Leu Lys Gln Val Tyr Ile
 325 330 335

Pro Thr Tyr Thr Lys Pro Asn Pro Asn Gln Ile Ile Ser Val Gly Ser
 340 345 350

Lys Pro Gly Met Asn Gly Ala Gly Phe Gln Lys Gly Leu Thr Cys Glu
 355 360 365

Ser Cys His Thr Thr Gln Ser Ala Gln Trp Tyr Ala Trp Gly Pro Pro
 370 375 380

Asn Met Gln Cys Arg Leu Cys Ala Ser Cys Trp Ile Tyr Trp Lys Lys
 385 390 395 400

Tyr Gly Gly Leu Lys Thr Pro Thr Gln Leu Glu Gly Ala Thr Arg Gly
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Thr Thr Glu Pro His Ser Arg Gly His Leu Ser Arg Pro Glu Ala Gln
 420 425 430

Ser Leu Ser Pro Tyr Thr Thr Ser Ala Asn Arg Ala Lys Leu Leu Ala
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Lys Asn Arg Gln Thr Phe Leu Leu Gln Thr Thr Lys Leu Thr Arg Leu
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Ala Arg Arg Met Cys Arg Asp Leu Leu Gln Pro Arg Arg Ala Ala Arg
 465 470 475 480

Arg Pro Tyr Ala Pro Ile Asn Ala Asn Ala Ile Lys Ala Glu Cys Ser
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Ile Arg Leu Pro Lys Ala Ala Lys Thr Pro Leu Lys Ile His Pro Leu
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Val Arg Leu Pro Leu Ala Thr Ile Val Lys Asp Leu Val Ala Gln Ala
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Pro Leu Lys Pro Lys Thr Pro Arg Gly Thr Lys Thr Pro Ile Asn Arg
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Asn Gln Leu Ser Gln Asn Arg Gly Leu Gly Gly Ile Met Val Lys Arg
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Ala Tyr Glu Thr Met Ala Gly Ala Gly Val Pro Phe Ser Ala Asn Gly
565 570 575

Arg Pro Leu Ala Ser Gly Ile Arg Ser Ser Ser Gln Pro Ala Ala Lys
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Arg Gln Lys Leu Asn Pro Ala Asp Ala Pro Asn Pro Val Val Phe Val
595 600 605

Ala Thr Lys Asp Thr Arg Ala Leu Arg Lys Ala Leu Thr His Leu Glu
610 615 620

Met Arg Arg Ala Ala Arg Arg Pro Asn Leu Pro Leu Lys Val Lys Pro
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<400> 151

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35 40 45

Asp Gly Asp Val Phe Arg Phe Pro Gly Leu Cys Asp Tyr Asn Phe Ala
 50 55 60

Ser Asp Cys Arg Gly Ser Tyr Lys Glu Phe Ala Val His Leu Lys Arg
 65 70 75 80

Gly Pro Gly Gln Ala Glu Ala Pro Ala Gly Val Glu Ser Ile Leu Leu
 85 90 95

Thr Ile Lys Asp Asp Thr Ile Tyr Leu Thr Arg His Leu Ala Val Leu
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Asn Gly Ala Val Val Ser Thr Pro His Tyr Ser Pro Gly Leu Leu Ile
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Glu Lys Ser Asp Ala Tyr Thr Lys Val Tyr Ser Arg Ala Gly Leu Thr
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Leu Met Trp Asn Arg Glu Asp Ala Leu Met Leu Glu Leu Asp Thr Lys
 145 150 155 160

Phe Arg Asn His Thr Cys Gly Leu Cys Gly Asp Tyr Asn Gly Leu Gln
 165 170 175

Ser Tyr Ser Glu Phe Leu Ser Asp Gly Val Leu Phe Ser Pro Leu Glu
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Phe Gly Asn Met Gln Lys Ile Asn Gln Pro Asp Val Val Cys Glu Asp
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Pro Glu Glu Glu Val Ala Pro Ala Ser Cys Ser Glu His Arg Ala Glu
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Cys Glu Arg Leu Leu Thr Ala Glu Ala Phe Ala Asp Cys Gln Asp Leu
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Val Pro Leu Glu Pro Tyr Leu Arg Ala Cys Gln Gln Asp Arg Cys Arg
 245 250 255

Cys Pro Gly Gly Asp Thr Cys Val Cys Ser Thr Val Ala Glu Phe Ser
 260 265 270

Arg Gln Cys Ser His Ala Gly Gly Arg Pro Gly Asn Trp Arg Thr Ala

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 Thr Leu Cys Pro Lys Thr Cys Pro Gly Asn Leu Val Tyr Leu Glu Ser
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 Gly Ser Pro Cys Met Asp Thr Cys Ser His Leu Glu Val Ser Ser Leu
 305 310 315 320
 Cys Glu Glu His Arg Met Asp Gly Cys Phe Cys Pro Glu Gly Thr Val
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 Tyr Asp Asp Ile Gly Asp Ser Gly Cys Val Pro Val Ser Gln Cys His
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 Cys Arg Leu His Gly His Leu Tyr Thr Pro Gly Gln Glu Ile Thr Asn
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 Asp Cys Glu Gln Cys Val Cys Asn Ala Gly Arg Trp Val Cys Lys Asp
 370 375 380
 Leu Pro Cys Pro Gly Thr Cys Ala Leu Glu Gly Gly Ser His Ile Thr
 385 390 395 400
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 Leu Ala Lys Gly Asp His Asn Asp Ser Tyr Ala Leu Leu Gly Glu Leu
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 Ser Val Leu Leu Asn Gln Leu Gln Val Asn Leu Pro His Val Thr Ala
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352/439

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Gln Thr Leu Ala Ala Gly Tyr Tyr His Thr Glu Cys Val Ser Gly Cys
785 790 795 800

Val Cys Pro Asp Gly Leu Met Asp Asp Gly Arg Gly Gly Cys Val Val
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Glu Lys Glu Cys Pro Cys Val His Asn Asn Asp Leu Tyr Ser Ser Gly
820 825 830

Ala Lys Ile Lys Val Asp Cys Asn Thr Cys Thr Cys Lys Arg Gly Arg
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Gly Val Thr Cys Ser Lys Ala Ile Lys Ile Phe Met Gly Arg Thr Glu
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Leu Lys Leu Glu Asp Lys His Arg Val Val Ile Gln Arg Asp Glu Gly
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His His Val Ala Tyr Thr Thr Arg Glu Val Gly Gln Tyr Leu Val Val
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Glu Ser Ser Thr Gly Ile Ile Val Ile Trp Asp Lys Arg Thr Thr Val
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Phe Ile Lys Leu Ala Pro Ser Tyr Lys Gly Thr Val Cys Gly Leu Cys
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PCT/US2004/000368

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 1865 1870 1875

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Thr Val	Thr Pro	Thr Pro	Thr Thr	Gly Thr
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 Ala Pro Ile Ala Glu Leu Thr Thr Ser Asn Pro Pro Pro Glu Ser
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 Ser Thr Pro Gln Thr Ser Arg Ser Thr Ser Ser Pro Leu Thr Glu
 4220 4225 4230
 Ser Thr Thr Leu Leu Ser Thr Leu Pro Pro Ala Ile Glu Met Thr
 4235 4240 4245
 Ser Thr Ala Pro Pro Ser Thr Pro Thr Ala Pro Thr Thr Thr Ser
 4250 4255 4260
 Gly Gly His Thr Leu Ser Pro Pro Pro Ser Thr Thr Thr Ser Pro
 4265 4270 4275
 Pro Gly Thr Pro Thr Arg Gly Thr Thr Thr Gly Ser Ser Ser Ala
 4280 4285 4290
 Pro Thr Pro Ser Thr Val Gln Thr Thr Thr Thr Ser Ala Trp Thr
 4295 4300 4305

Pro Thr Pro Thr Pro Leu Ser Thr Pro Ser Ile Ile Arg Thr Thr
 4310 4315 4320
 Gly Leu Arg Pro Tyr Pro Ser Ser Val Leu Ile Cys Cys Val Leu
 4325 4330 4335
 Asn Asp Thr Tyr Tyr Ala Pro Gly Glu Glu Val Tyr Asn Gly Thr
 4340 4345 4350
 Tyr Gly Asp Thr Cys Tyr Phe Val Asn Cys Ser Leu Ser Cys Thr
 4355 4360 4365
 Leu Glu Phe Tyr Asn Trp Ser Cys Pro Ser Thr Pro Ser Pro Thr
 4370 4375 4380
 Pro Thr Pro Ser Lys Ser Thr Pro Thr Pro Ser Lys Pro Ser Ser
 4385 4390 4395
 Thr Pro Ser Lys Pro Thr Pro Gly Thr Lys Pro Pro Glu Cys Pro
 4400 4405 4410
 Asp Phe Asp Pro Pro Arg Gln Glu Asn Glu Thr Trp Trp Leu Cys
 4415 4420 4425
 Asp Cys Phe Met Ala Thr Cys Lys Tyr Asn Asn Thr Val Glu Ile
 4430 4435 4440
 Val Lys Val Glu Cys Glu Pro Pro Pro Met Pro Thr Cys Ser Asn
 4445 4450 4455
 Gly Leu Gln Pro Val Arg Val Glu Asp Pro Asp Gly Cys Cys Trp
 4460 4465 4470
 His Trp Glu Cys Asp Cys Tyr Cys Thr Gly Trp Gly Asp Pro His
 4475 4480 4485
 Tyr Val Thr Phe Asp Gly Leu Tyr Tyr Ser Tyr Gln Gly Asn Cys
 4490 4495 4500
 Thr Tyr Val Leu Val Glu Glu Ile Ser Pro Ser Val Asp Asn Phe
 4505 4510 4515
 Gly Val Tyr Ile Asp Asn Tyr His Cys Asp Pro Asn Asp Lys Val
 4520 4525 4530

Ser Cys Pro Arg Thr Leu Ile Val Arg His Glu Thr Gln Glu Val
 4535 4540 4545
 Leu Ile Lys Thr Val His Met Met Pro Met Gln Val Gln Val Gln
 4550 4555 4560
 Val Asn Arg Gln Ala Val Ala Leu Pro Tyr Lys Lys Tyr Gly Leu
 4565 4570 4575
 Glu Val Tyr Gln Ser Gly Ile Asn Tyr Val Val Asp Ile Pro Glu
 4580 4585 4590
 Leu Gly Val Leu Val Ser Tyr Asn Gly Leu Ser Phe Ser Val Arg
 4595 4600 4605
 Leu Pro Tyr His Arg Phe Gly Asn Asn Thr Lys Gly Gln Cys Gly
 4610 4615 4620
 Thr Cys Thr Asn Thr Thr Ser Asp Asp Cys Ile Leu Pro Ser Gly
 4625 4630 4635
 Glu Ile Val Ser Asn Cys Glu Ala Ala Ala Asp Gln Trp Leu Val
 4640 4645 4650
 Asn Asp Pro Ser Lys Pro His Cys Pro His Ser Ser Ser Thr Thr
 4655 4660 4665
 Lys Arg Pro Ala Val Thr Val Pro Gly Gly Gly Lys Thr Thr Pro
 4670 4675 4680
 His Lys Asp Cys Thr Pro Ser Pro Leu Cys Gln Leu Ile Lys Asp
 4685 4690 4695
 Ser Leu Phe Ala Gln Cys His Ala Leu Val Pro Pro Gln His Tyr
 4700 4705 4710
 Tyr Asp Ala Cys Val Phe Asp Ser Cys Phe Met Pro Gly Ser Ser
 4715 4720 4725
 Leu Glu Cys Ala Ser Leu Gln Ala Tyr Ala Ala Leu Cys Ala Gln
 4730 4735 4740
 Gln Asn Ile Cys Leu Asp Trp Arg Asn His Thr His Gly Ala Cys

4745		4750		4755
Leu Val Glu Cys Pro Ser His Arg Glu Tyr Gln Ala Cys Gly Pro				
4760		4765		4770
Ala Glu Glu Pro Thr Cys Lys Ser Ser Ser Ser Gln Gln Asn Asn				
4775		4780		4785
Thr Val Leu Val Glu Gly Cys Phe Cys Pro Glu Gly Thr Met Asn				
4790		4795		4800
Tyr Ala Pro Gly Phe Asp Val Cys Val Lys Thr Cys Gly Cys Val				
4805		4810		4815
Gly Pro Asp Asn Val Pro Arg Glu Phe Gly Glu His Phe Glu Phe				
4820		4825		4830
Asp Cys Lys Asn Cys Val Cys Leu Glu Gly Gly Ser Gly Ile Ile				
4835		4840		4845
Cys Gln Pro Lys Arg Cys Ser Gln Lys Pro Val Thr His Cys Val				
4850		4855		4860
Glu Asp Gly Thr Tyr Leu Ala Thr Glu Val Asn Pro Ala Asp Thr				
4865		4870		4875
Cys Cys Asn Ile Thr Val Cys Lys Cys Asn Thr Ser Leu Cys Lys				
4880		4885		4890
Glu Lys Pro Ser Val Cys Pro Leu Gly Phe Glu Val Lys Ser Lys				
4895		4900		4905
Met Val Pro Gly Arg Cys Cys Pro Phe Tyr Trp Cys Glu Ser Lys				
4910		4915		4920
Gly Val Cys Val His Gly Asn Ala Glu Tyr Gln Pro Gly Ser Pro				
4925		4930		4935
Val Tyr Ser Ser Lys Cys Gln Asp Cys Val Cys Thr Asp Lys Val				
4940		4945		4950
Asp Asn Asn Thr Leu Leu Asn Val Ile Ala Cys Thr His Val Pro				
4955		4960		4965

Cys Asn Thr Ser Cys Ser Pro Gly Phe Glu Leu Met Glu Ala Pro
 4970 4975 4980

Gly Glu Cys Cys Lys Lys Cys Glu Gln Thr His Cys Ile Ile Lys
 4985 4990 4995

Arg Pro Asp Asn Gln His Val Ile Leu Lys Pro Gly Asp Phe Lys
 5000 5005 5010

Ser Asp Pro Lys Asn Asn Cys Thr Phe Phe Ser Cys Val Lys Ile
 5015 5020 5025

His Asn Gln Leu Ile Ser Ser Val Ser Asn Ile Thr Cys Pro Asn
 5030 5035 5040

Phe Asp Ala Ser Ile Cys Ile Pro Gly Ser Ile Thr Phe Met Pro
 5045 5050 5055

Asn Gly Cys Cys Lys Thr Cys Thr Pro Arg Asn Glu Thr Arg Val
 5060 5065 5070

Pro Cys Ser Thr Val Pro Val Thr Thr Glu Val Ser Tyr Ala Gly
 5075 5080 5085

Cys Thr Lys Thr Val Leu Met Asn His Cys Ser Gly Ser Cys Gly
 5090 5095 5100

Thr Phe Val Met Tyr Ser Ala Lys Ala Gln Ala Leu Asp His Ser
 5105 5110 5115

Cys Ser Cys Cys Lys Glu Glu Lys Thr Ser Gln Arg Glu Val Val
 5120 5125 5130

Leu Ser Cys Pro Asn Gly Gly Ser Leu Thr His Thr Tyr Thr His
 5135 5140 5145

Ile Glu Ser Cys Gln Cys Gln Asp Thr Val Cys Gly Leu Pro Thr
 5150 5155 5160

Gly Thr Ser Arg Arg Ala Arg Arg Ser Pro Arg His Leu Gly Ser
 5165 5170 5175

Gly

<210> 152
 <211> 878
 <212> PRT
 <213> Human

<400> 152

Thr Ile Tyr Ser Thr Val Ser Ser Ser Thr Thr Ala Ile Thr Ser Pro
 1 5 10 15

Phe Thr Thr Ala Glu Thr Gly Val Thr Ser Thr Pro Ser Ser Pro Ser
 20 25 30

Ser Leu Ser Thr Asp Ile Pro Thr Thr Ser Leu Arg Thr Leu Thr Pro
 35 40 45

Leu Ser Leu Ser Thr Ser Thr Ser Leu Thr Thr Thr Thr Asp Leu Pro
 50 55 60

Ser Ile Pro Thr Asp Ile Ser Ser Leu Pro Thr Pro Ile His Ile Ile
 65 70 75 80

Ser Ser Ser Pro Ser Ile Gln Ser Thr Glu Thr Ser Ser Leu Val Gly
 85 90 95

Thr Thr Ser Pro Thr Met Ser Thr Val Arg Ala Thr Leu Arg Ser Thr
 100 105 110

Glu Asn Thr Pro Ile Ser Ser Phe Ser Thr Ser Ile Val Val Thr Pro
 115 120 125

Glu Thr Pro Thr Thr Gln Ala Pro Pro Val Leu Met Ser Ala Thr Gly
 130 135 140

Thr Gln Thr Ser Pro Val Pro Thr Thr Val Thr Phe Gly Ser Met Asp
 145 150 155 160

Ser Ser Thr Ser Thr Leu His Thr Leu Thr Pro Ser Thr Ala Leu Ser
 165 170 175

Lys Ile Met Ser Thr Ser Gln Phe Pro Ile Pro Ser Thr His Ser Ser
 180 185 190

Thr Leu Gln Thr Thr Pro Ser Ile Pro Ser Leu Gln Thr Ser Leu Thr
 195 200 205

Ser Thr Ser Glu Phe Thr Thr Glu Ser Phe Thr Arg Gly Ser Thr Ser
 210 215 220

Thr Asn Ala Ile Leu Thr Ser Phe Ser Thr Ile Ile Trp Ser Ser Thr
 225 230 235 240

Pro Thr Ile Ile Met Ser Ser Ser Pro Ser Ser Ala Ser Ile Thr Pro
 245 250 255

Val Phe Ala Thr Thr Ile His Ser Val Pro Ser Ser Pro Tyr Ile Phe
 260 265 270

Ser Thr Glu Asn Val Gly Ser Ala Ser Ile Thr Ala Phe Pro Ser Leu
 275 280 285

Ser Ser Ser Ser Thr Thr Ser Thr Ser Pro Thr Ser Ser Ser Leu Thr
 290 295 300

Thr Ala Leu Thr Glu Ile Thr Pro Phe Ser Tyr Ile Ser Leu Pro Ser
 305 310 315 320

Thr Thr Pro Cys Pro Gly Thr Ile Thr Ile Thr Ile Val Pro Ala Ser
 325 330 335

Pro Thr Asp Pro Cys Val Glu Met Asp Pro Ser Thr Glu Ala Thr Ser
 340 345 350

Pro Pro Thr Thr Pro Leu Thr Val Phe Pro Phe Thr Thr Glu Met Val
 355 360 365

Thr Cys Pro Ser Ser Ile Ser Met Gln Thr Thr Leu Ala Thr His Met
 370 375 380

Asp Thr Ser Ser Met Thr Pro Glu Ser Glu Ser Ser Ile Ile Pro Asn
 385 390 395 400

Ala Ser Ser Ser Thr Gly Thr Gly Thr Val Pro Thr Asn Thr Val Phe
 405 410 415

Thr Ser Thr Arg Leu Pro Thr Ser Glu Thr Trp Leu Ser Asn Asn Ser
 420 425 430

Val Ile Pro Thr Pro Leu Pro Gly Val Ser Thr Ile Pro Leu Thr Met
 435 440 445

Lys Pro Ser Ser Ser Leu Pro Thr Ile Leu Arg Thr Ser Ser Lys Ser
 450 455 460

Thr His Pro Ser Pro Pro Thr Ala Arg Thr Ser Glu Thr Ser Val Ala
 465 470 475 480

Thr Thr Gln Thr Pro Thr Thr Leu Thr Thr Arg Arg Thr Thr Pro Ile
 485 490 495

Thr Ser Trp Met Thr Thr Gln Ser Thr Leu Thr Thr Thr Ala Gly Thr
 500 505 510

Cys Asp Asn Gly Gly Thr Trp Glu Gln Gly Gln Cys Ala Cys Leu Pro
 515 520 525

Gly Phe Ser Gly Asp Arg Cys Gln Leu Gln Thr Arg Cys Gln Asn Gly
 530 535 540

Gly Gln Trp Asp Gly Leu Lys Cys Gln Cys Pro Ser Thr Phe Tyr Gly
 545 550 555 560

Ser Ser Cys Glu Phe Ala Val Glu Gln Val Asp Leu Asp Val Val Glu
 565 570 575

Thr Glu Val Gly Met Glu Val Ser Val Asp Gln Gln Phe Ser Pro Asp
 580 585 590

Leu Asn Asp Asn Thr Ser Gln Ala Tyr Arg Asp Phe Asn Lys Thr Phe
 595 600 605

Trp Asn Gln Met Gln Lys Ile Phe Ala Asp Met Gln Gly Phe Thr Phe
 610 615 620

Lys Gly Val Glu Ile Leu Ser Leu Arg Asn Gly Ser Ile Val Val Asp
 625 630 635 640

Tyr Leu Val Leu Leu Glu Met Pro Phe Ser Pro Gln Leu Glu Ser Glu
 645 650 655

Tyr Glu Gln Val Lys Thr Thr Leu Lys Glu Gly Leu Gln Asn Ala Ser
 660 665 670

Gln Asp Ala Asn Ser Cys Gln Asp Ser Gln Thr Leu Cys Phe Lys Pro

675 680 685
 Asp Ser Ile Lys Val Asn Asn Asn Ser Lys Thr Glu Leu Thr Pro Glu
 690 695 700
 Ala Ile Cys Arg Arg Ala Ala Pro Thr Gly Tyr Glu Glu Phe Tyr Phe
 705 710 715 720
 Pro Leu Val Glu Ala Thr Arg Leu Arg Cys Val Thr Lys Cys Thr Ser
 725 730 735
 Gly Val Asp Asn Ala Ile Asp Cys His Gln Gly Gln Cys Val Leu Glu
 740 745 750
 Thr Ser Gly Pro Ala Cys Arg Cys Tyr Ser Thr Asp Thr His Trp Phe
 755 760 765
 Ser Gly Pro Arg Cys Glu Val Ala Val His Trp Arg Ala Leu Val Gly
 770 775 780
 Gly Leu Thr Ala Gly Ala Ala Leu Leu Val Leu Leu Leu Leu Ala Leu
 785 790 795 800
 Gly Val Arg Ala Val Arg Ser Gly Trp Trp Gly Gly Gln Arg Arg Gly
 805 810 815
 Arg Ser Trp Asp Gln Asp Arg Lys Trp Phe Glu Thr Trp Asp Glu Glu
 820 825 830
 Val Val Gly Thr Phe Ser Asn Trp Gly Phe Glu Asp Asp Gly Thr Asp
 835 840 845
 Lys Asp Thr Asn Phe His Val Ala Leu Glu Asn Val Asp Thr Thr Met
 850 855 860
 Lys Val His Ile Lys Arg Pro Glu Met Thr Ser Ser Ser Val
 865 870 875
 <210> 153
 <211> 1938
 <212> PRT
 <213> Human
 <400> 153
 Met Ser Ser Asp Ala Glu Met Ala Ile Phe Gly Glu Ala Ala Pro Tyr

ALL

Asp Asn Ser Ser Arg Phe Gly Lys Phe Ile Arg Ile His Phe Gly Ala
 245 250 255
 Thr Gly Lys Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu Glu Lys
 260 265 270
 Ser Arg Val Thr Phe Gln Leu Ser Ser Glu Arg Ser Tyr His Ile Phe
 275 280 285
 Tyr Gln Ile Met Ser Asn Lys Lys Pro Glu Leu Ile Asp Leu Leu Leu
 290 295 300
 Ile Ser Thr Asn Pro Phe Asp Phe Pro Phe Val Ser Gln Gly Glu Val
 305 310 315 320
 Thr Val Ala Ser Ile Asp Asp Ser Glu Glu Leu Leu Ala Thr Asp Asn
 325 330 335
 Ala Ile Asp Ile Leu Gly Phe Ser Ser Glu Glu Lys Val Gly Ile Tyr
 340 345 350
 Lys Leu Thr Gly Ala Val Met His Tyr Gly Asn Met Lys Phe Lys Gln
 355 360 365
 Lys Gln Arg Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Val Ala Asp
 370 375 380
 Lys Ala Gly Tyr Leu Met Gly Leu Asn Ser Ala Glu Met Leu Lys Gly
 385 390 395 400
 Leu Cys Cys Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly
 405 410 415
 Gln Asn Val Gln Gln Val Thr Asn Ser Val Gly Ala Leu Ala Lys Ala
 420 425 430
 Val Tyr Glu Lys Met Phe Leu Trp Met Val Thr Arg Ile Asn Gln Gln
 435 440 445
 Leu Asp Thr Lys Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile
 450 455 460
 Ala Gly Phe Glu Ile Phe Asp Phe Asn Ser Leu Glu Gln Leu Cys Ile
 465 470 475 480

Asn Phe Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe
 485 490 495
 Val Leu Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Glu Phe
 500 505 510
 Ile Asp Phe Gly Met Asp Leu Ala Ala Cys Ile Glu Leu Ile Glu Lys
 515 520 525
 Pro Met Gly Ile Phe Ser Ile Leu Glu Glu Glu Cys Met Phe Pro Lys
 530 535 540
 Ala Thr Asp Thr Ser Phe Lys Asn Lys Leu Tyr Asp Gln His Leu Gly
 545 550 555 560
 Lys Ser Asn Asn Phe Gln Lys Pro Lys Pro Ala Lys Gly Lys Ala Glu
 565 570 575
 Ala His Phe Ser Leu Val His Tyr Ala Gly Thr Val Asp Tyr Asn Ile
 580 585 590
 Ala Gly Trp Leu Asp Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val
 595 600 605
 Gly Leu Tyr Gln Lys Ser Ser Leu Lys Leu Leu Ser Phe Leu Phe Ser
 610 615 620
 Asn Tyr Ala Gly Ala Glu Thr Gly Asp Ser Gly Gly Ser Lys Lys Gly
 625 630 635 640
 Gly Lys Lys Lys Gly Ser Ser Phe Gln Thr Val Ser Ala Val Phe Arg
 645 650 655
 Glu Asn Leu Asn Lys Leu Met Thr Asn Leu Arg Ser Thr His Pro His
 660 665 670
 Phe Val Arg Cys Leu Ile Pro Asn Glu Thr Lys Thr Pro Gly Val Met
 675 680 685
 Asp His Tyr Leu Val Met His Gln Leu Arg Cys Asn Gly Val Leu Glu
 690 695 700
 Gly Ile Arg Ile Cys Arg Lys Gly Phe Pro Ser Arg Ile Leu Tyr Ala
 705 710 715 720

Asp Phe Lys Gln Arg Tyr Arg Ile Leu Asn Ala Ser Ala Ile Pro Glu
 725 730 735

Gly Gln Phe Ile Asp Ser Lys Asn Ala Ser Glu Lys Leu Leu Asn Ser
 740 745 750

Ile Asp Val Asp Arg Glu Gln Phe Arg Phe Gly Asn Thr Lys Val Phe
 755 760 765

Phe Lys Ala Gly Leu Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Lys
 770 775 780

Leu Val Thr Leu Met Thr Ser Thr Gln Ala Val Cys Arg Gly Tyr Leu
 785 790 795 800

Met Arg Val Glu Phe Lys Lys Met Met Glu Arg Arg Asp Ser Ile Phe
 805 810 815

Cys Ile Gln Tyr Asn Ile Arg Ser Phe Met Asn Val Lys His Trp Pro
 820 825 830

Trp Met Asn Leu Phe Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu
 835 840 845

Ala Glu Lys Glu Met Ala Thr Met Lys Glu Asp Phe Glu Arg Thr Lys
 850 855 860

Glu Glu Leu Ala Arg Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys
 865 870 875 880

Met Val Ser Leu Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln
 885 890 895

Ser Glu Thr Glu Asn Leu Met Asp Ala Glu Glu Arg Cys Glu Gly Leu
 900 905 910

Ile Lys Ser Lys Ile Leu Leu Glu Ala Lys Val Lys Glu Leu Thr Glu
 915 920 925

Arg Leu Glu Glu Glu Glu Glu Met Asn Ser Glu Leu Val Ala Lys Lys
 930 935 940

Arg Asn Leu Glu Asp Lys Cys Ser Ser Leu Lys Arg Asp Ile Asp Asp

945	950	955	960
Leu Glu Leu Thr	Leu Thr Lys Val Glu Lys Glu Lys His Ala Thr Glu		
	965	970	975
Asn Lys Val Lys Asn Leu Ser Glu Glu Met Thr Ala Leu Glu Glu Asn			
	980	985	990
Ile Ser Lys Leu Thr Lys Glu Lys Lys Ser Leu Gln Glu Ala His Gln			
	995	1000	1005
Gln Thr Leu Asp Asp Leu Gln Val Glu Glu Asp Lys Val Asn Gly			
	1010	1015	1020
Leu Ile Lys Ile Asn Ala Lys Leu Glu Gln Gln Thr Asp Asp Leu			
	1025	1030	1035
Glu Gly Ser Leu Glu Gln Glu Lys Lys Leu Arg Ala Asp Leu Glu			
	1040	1045	1050
Arg Ala Lys Arg Lys Leu Glu Gly Asp Leu Lys Met Ser Gln Glu			
	1055	1060	1065
Ser Ile Met Asp Leu Glu Asn Glu Lys Gln Gln Ile Glu Glu Lys			
	1070	1075	1080
Leu Lys Lys Lys Glu Phe Glu Leu Ser Gln Leu Gln Ala Arg Ile			
	1085	1090	1095
Asp Asp Glu Gln Val His Ser Leu Gln Phe Gln Lys Lys Ile Lys			
	1100	1105	1110
Glu Leu Gln Ala Arg Ile Glu Glu Leu Glu Glu Glu Ile Glu Ala			
	1115	1120	1125
Glu His Thr Leu Arg Ala Lys Ile Glu Lys Gln Arg Ser Asp Leu			
	1130	1135	1140
Ala Arg Glu Leu Glu Glu Ile Ser Glu Arg Leu Glu Glu Ala Ser			
	1145	1150	1155
Gly Ala Thr Ser Ala Gln Ile Glu Met Asn Lys Lys Arg Glu Ala			
	1160	1165	1170

Glu Phe Gln Lys Met Arg Arg Asp Leu Glu Glu Ala Thr Leu Gln
 1175 1180 1185
 His Glu Ala Thr Ala Ala Thr Leu Arg Lys Lys Gln Ala Asp Ser
 1190 1195 1200
 Val Ala Glu Leu Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys
 1205 1210 1215
 Gln Lys Leu Glu Lys Glu Lys Ser Glu Leu Lys Met Glu Ile Asp
 1220 1225 1230
 Asp Met Ala Ser Asn Ile Glu Ala Leu Ser Lys Ser Lys Ser Asn
 1235 1240 1245
 Ile Glu Arg Thr Cys Arg Thr Val Glu Asp Gln Phe Ser Glu Ile
 1250 1255 1260
 Lys Ala Lys Asp Glu Gln Gln Thr Gln Leu Ile His Asp Leu Asn
 1265 1270 1275
 Met Gln Lys Ala Arg Leu Gln Thr Gln Asn Gly Glu Leu Ser His
 1280 1285 1290
 Arg Val Glu Glu Lys Glu Ser Leu Ile Ser Gln Leu Thr Lys Ser
 1295 1300 1305
 Lys Gln Ala Leu Thr Gln Gln Leu Glu Glu Leu Lys Arg Gln Met
 1310 1315 1320
 Glu Glu Glu Thr Lys Ala Lys Asn Ala Met Ala His Ala Leu Gln
 1325 1330 1335
 Ser Ser Arg His Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu
 1340 1345 1350
 Glu Gln Glu Ala Lys Ala Glu Leu Gln Arg Ala Leu Ser Lys Ala
 1355 1360 1365
 Asn Ser Glu Val Ala Gln Trp Lys Thr Lys Tyr Glu Thr Asp Ala
 1370 1375 1380
 Ile Gln Arg Thr Glu Glu Leu Glu Glu Ala Lys Lys Lys Leu Ala
 1385 1390 1395

Gln Arg	Leu Gln Glu Ala Glu	Glu Lys Thr Glu Thr	Ala Asn Ser
1400	1405	1410	
Lys Cys	Ala Ser Leu Glu Lys	Thr Lys Gln Arg Leu	Gln Gly Glu
1415	1420	1425	
Val Glu	Asp Leu Met Arg Asp	Leu Glu Arg Ser His	Thr Ala Cys
1430	1435	1440	
Ala Thr	Leu Asp Lys Lys Gln	Arg Asn Phe Asp Lys	Val Leu Ala
1445	1450	1455	
Glu Trp	Lys Gln Lys Leu Asp	Glu Ser Gln Ala Glu	Leu Glu Ala
1460	1465	1470	
Ala Gln	Lys Glu Ser Arg Ser	Leu Ser Thr Glu Leu	Phe Lys Met
1475	1480	1485	
Arg Asn	Ala Tyr Glu Glu Val	Val Asp Gln Leu Glu	Thr Leu Arg
1490	1495	1500	
Arg Glu	Asn Lys Asn Leu Gln	Glu Glu Ile Ser Asp	Leu Thr Glu
1505	1510	1515	
Gln Ile	Ala Glu Thr Gly Lys	Asn Leu Gln Glu Ala	Glu Lys Thr
1520	1525	1530	
Lys Lys	Leu Val Glu Gln Glu	Lys Ser Asp Leu Gln	Val Ala Leu
1535	1540	1545	
Glu Glu	Val Glu Gly Ser Leu	Glu His Glu Glu Ser	Lys Ile Leu
1550	1555	1560	
Arg Val	Gln Leu Glu Leu Ser	Gln Val Lys Ser Glu	Leu Asp Arg
1565	1570	1575	
Lys Val	Ile Glu Lys Asp Glu	Glu Ile Glu Gln Leu	Lys Arg Asn
1580	1585	1590	
Ser Gln	Arg Ala Ala Glu Ala	Leu Gln Ser Val Leu	Asp Ala Glu
1595	1600	1605	
Ile Arg	Ser Arg Asn Asp Ala	Leu Arg Leu Lys Lys	Lys Met Glu
1610	1615	1620	

Gly Asp Leu Asn Glu Met Glu Ile Gln Leu Gly His Ser Asn Arg
 1625 1630 1635

Gln Met Ala Glu Thr Gln Arg His Leu Arg Thr Val Gln Gly Gln
 1640 1645 1650

Leu Lys Asp Ser Gln Leu His Leu Asp Asp Ala Leu Arg Ser Asn
 1655 1660 1665

Glu Asp Leu Lys Glu Gln Leu Ala Ile Val Glu Arg Arg Asn Gly
 1670 1675 1680

Leu Leu Leu Glu Glu Leu Glu Glu Met Lys Val Ala Leu Glu Gln
 1685 1690 1695

Thr Glu Arg Thr Arg Arg Leu Ser Glu Gln Glu Leu Leu Asp Ala
 1700 1705 1710

Ser Asp Arg Val Gln Leu Leu His Ser Gln Asn Thr Ser Leu Ile
 1715 1720 1725

Asn Thr Lys Lys Lys Leu Glu Ala Asp Ile Ala Gln Cys Gln Ala
 1730 1735 1740

Glu Val Glu Asn Ser Ile Gln Glu Ser Arg Asn Ala Glu Glu Lys
 1745 1750 1755

Ala Lys Lys Ala Ile Thr Asp Ala Ala Met Met Ala Glu Glu Leu
 1760 1765 1770

Lys Lys Glu Gln Asp Thr Ser Ala His Leu Glu Arg Met Lys Lys
 1775 1780 1785

Asn Leu Glu Gln Thr Val Lys Asp Leu Gln His Arg Leu Asp Glu
 1790 1795 1800

Ala Glu Gln Leu Ala Leu Lys Gly Gly Lys Lys Gln Ile Gln Lys
 1805 1810 1815

Leu Glu Asn Arg Val Arg Glu Leu Glu Asn Glu Leu Asp Val Glu
 1820 1825 1830

Gln Lys Arg Gly Ala Glu Ala Leu Lys Gly Ala His Lys Tyr Glu

1835 1840 1845
 Arg Lys Val Lys Glu Met Thr Tyr Gln Ala Glu Glu Asp Arg Lys
 1850 1855 1860
 Asn Ile Leu Arg Leu Gln Asp Leu Val Asp Lys Leu Gln Ala Lys
 1865 1870 1875
 Val Lys Ser Tyr Lys Arg Gln Ala Glu Glu Ala Glu Glu Gln Ala
 1880 1885 1890
 Asn Thr Gln Leu Ser Arg Cys Arg Arg Val Gln His Glu Leu Glu
 1895 1900 1905
 Glu Ala Ala Glu Arg Ala Asp Ile Ala Glu Ser Gln Val Asn Lys
 1910 1915 1920
 Leu Arg Ala Lys Ser Arg Asp Val Gly Ser Gln Lys Met Glu Glu
 1925 1930 1935

 <210> 154
 <211> 173
 <212> PRT
 <213> Human

 <400> 154
 Met Ala Ser Arg Lys Thr Lys Lys Lys Glu Gly Gly Ala Leu Arg Ala
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 Gln Arg Ala Ser Ser Asn Val Phe Ser Asn Phe Glu Gln Thr Gln Ile
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 Gln Glu Phe Lys Glu Ala Phe Thr Leu Met Asp Gln Asn Arg Asp Gly
 35 40 45
 Phe Ile Asp Lys Glu Asp Leu Lys Asp Thr Tyr Ala Ser Leu Gly Lys
 50 55 60
 Thr Asn Val Lys Asp Asp Glu Leu Asp Ala Met Leu Lys Glu Ala Ser
 65 70 75 80
 Gly Pro Ile Asn Phe Thr Met Phe Leu Asn Leu Phe Gly Glu Lys Leu
 85 90 95
 Ser Gly Thr Asp Ala Glu Glu Thr Ile Leu Asn Ala Phe Lys Met Leu

100 105 110
 Asp Pro Asp Gly Lys Gly Lys Ile Asn Lys Glu Tyr Ile Lys Arg Leu
 115 120 125
 Leu Met Ser Gln Ala Asp Lys Met Thr Ala Glu Glu Val Asp Gln Met
 130 135 140
 Phe Gln Phe Ala Ser Ile Asp Val Ala Gly Asn Leu Asp Tyr Lys Ala
 145 150 155 160
 Leu Ser Tyr Val Ile Thr His Gly Glu Glu Lys Glu Glu
 165 170
 <210> 155
 <211> 984
 <212> PRT
 <213> Human
 <400> 155
 Met Glu Thr Lys Gly Tyr His Ser Leu Pro Glu Gly Leu Asp Met Glu
 1 5 10 15
 Arg Arg Trp Gly Gln Val Ser Gln Ala Val Glu Arg Ser Ser Leu Gly
 20 25 30
 Pro Thr Glu Arg Thr Asp Glu Asn Asn Tyr Met Glu Ile Val Asn Val
 35 40 45
 Ser Cys Val Ser Gly Ala Ile Pro Asn Asn Ser Thr Gln Gly Ser Ser
 50 55 60
 Lys Glu Lys Gln Glu Leu Leu Pro Cys Leu Gln Gln Asp Asn Asn Arg
 65 70 75 80
 Pro Gly Ile Leu Thr Ser Asp Ile Lys Thr Glu Leu Glu Ser Lys Glu
 85 90 95
 Leu Ser Ala Thr Val Ala Gly Ser Met Gly Leu Tyr Met Asp Ser Val
 100 105 110
 Arg Asp Ala Asp Tyr Ser Tyr Glu Gln Gln Asn Gln Gln Gly Ser Met
 115 120 125
 Ser Pro Ala Lys Ile Tyr Gln Asn Val Glu Gln Leu Val Lys Phe Tyr

130 135 140
 Lys Gly Asn Gly His Arg Pro Ser Thr Leu Ser Cys Val Asn Thr Pro
 145 150 155 160
 Leu Arg Ser Phe Met Ser Asp Ser Gly Ser Ser Val Asn Gly Gly Val
 165 170 175
 Met Arg Ala Ile Val Lys Ser Pro Ile Met Cys His Glu Lys Ser Pro
 180 185 190
 Ser Val Cys Ser Pro Leu Asn Met Thr Ser Ser Val Cys Ser Pro Ala
 195 200 205
 Gly Ile Asn Ser Val Ser Ser Thr Thr Ala Ser Phe Gly Ser Phe Pro
 210 215 220
 Val His Ser Pro Ile Thr Gln Gly Thr Pro Leu Thr Cys Ser Pro Asn
 225 230 235 240
 Ala Glu Asn Arg Gly Ser Arg Ser His Ser Pro Ala His Ala Ser Asn
 245 250 255
 Val Gly Ser Pro Leu Ser Ser Pro Leu Ser Ser Met Lys Ser Ser Ile
 260 265 270
 Ser Ser Pro Pro Ser His Cys Ser Val Lys Ser Pro Val Ser Ser Pro
 275 280 285
 Asn Asn Val Thr Leu Arg Ser Ser Val Ser Ser Pro Ala Asn Ile Asn
 290 295 300
 Asn Ser Arg Cys Ser Val Ser Ser Pro Ser Asn Thr Asn Asn Arg Ser
 305 310 315 320
 Thr Leu Ser Ser Pro Ala Ala Ser Thr Val Gly Ser Ile Cys Ser Pro
 325 330 335
 Val Asn Asn Ala Phe Ser Tyr Thr Ala Ser Gly Thr Ser Ala Gly Ser
 340 345 350
 Ser Thr Leu Arg Asp Val Val Pro Ser Pro Asp Thr Gln Glu Lys Gly
 355 360 365

Ala Gln Glu Val Pro Phe Pro Lys Thr Glu Glu Val Glu Ser Ala Ile
 370 375 380

Ser Asn Gly Val Thr Gly Gln Leu Asn Ile Val Gln Tyr Ile Lys Pro
 385 390 395 400

Glu Pro Asp Gly Ala Phe Ser Ser Ser Cys Leu Gly Gly Asn Ser Lys
 405 410 415

Ile Asn Ser Asp Ser Ser Phe Ser Val Pro Ile Lys Gln Glu Ser Thr
 420 425 430

Lys His Ser Cys Ser Gly Thr Ser Phe Lys Gly Asn Pro Thr Val Asn
 435 440 445

Pro Phe Pro Phe Met Asp Gly Ser Tyr Phe Ser Phe Met Asp Asp Lys
 450 455 460

Asp Tyr Tyr Ser Leu Ser Gly Ile Leu Gly Pro Pro Val Pro Gly Phe
 465 470 475 480

Asp Gly Asn Cys Glu Gly Ser Gly Phe Pro Val Gly Ile Lys Gln Glu
 485 490 495

Pro Asp Asp Gly Ser Tyr Tyr Pro Glu Ala Ser Ile Pro Ser Ser Ala
 500 505 510

Ile Val Gly Val Asn Ser Gly Gly Gln Ser Phe His Tyr Arg Ile Gly
 515 520 525

Ala Gln Gly Thr Ile Ser Leu Ser Arg Ser Ala Arg Asp Gln Ser Phe
 530 535 540

Gln His Leu Ser Ser Phe Pro Pro Val Asn Thr Leu Val Glu Ser Trp
 545 550 555 560

Lys Ser His Gly Asp Leu Ser Ser Arg Arg Ser Asp Gly Tyr Pro Val
 565 570 575

Leu Glu Tyr Ile Pro Glu Asn Val Ser Ser Ser Thr Leu Arg Ser Val
 580 585 590

Ser Thr Gly Ser Ser Arg Pro Ser Lys Ile Cys Leu Val Cys Gly Asp
 595 600 605

...

Glu Ala Ser Gly Cys His Tyr Gly Val Val Thr Cys Gly Ser Cys Lys
 610 615 620

Val Phe Phe Lys Arg Ala Val Glu Gly Gln His Asn Tyr Leu Cys Ala
 625 630 635 640

Gly Arg Asn Asp Cys Ile Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro
 645 650 655

Ala Cys Arg Leu Gln Lys Cys Leu Gln Ala Gly Met Asn Leu Gly Ala
 660 665 670

Arg Lys Ser Lys Lys Leu Gly Lys Leu Lys Gly Ile His Glu Glu Gln
 675 680 685

Pro Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Gln Ser Pro
 690 695 700

Glu Glu Gly Thr Thr Tyr Ile Ala Pro Ala Lys Glu Pro Ser Val Asn
 705 710 715 720

Thr Ala Leu Val Pro Gln Leu Ser Thr Ile Ser Arg Ala Leu Thr Pro
 725 730 735

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
 740 745 750

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
 755 760 765

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
 770 775 780

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
 785 790 795 800

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
 805 810 815

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
 820 825 830

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
 835 840 845

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
850 855 860

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
865 870 875 880

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
885 890 895

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
900 905 910

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
915 920 925

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
930 935 940

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
945 950 955 960

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
965 970 975

Lys Pro Leu Tyr Phe His Arg Lys
980

<210> 156
<211> 495
<212> PRT
<213> Human

<400> 156

Met Ser Ser Asn Ser Asp Thr Gly Asp Leu Gln Glu Ser Leu Lys His
1 5 10 15

Gly Leu Thr Pro Ile Val Ser Gln Phe Lys Met Val Asn Tyr Ser Tyr
20 25 30

Asp Glu Asp Leu Glu Glu Leu Cys Pro Val Cys Gly Asp Lys Val Ser
35 40 45

Gly Tyr His Tyr Gly Leu Leu Thr Cys Glu Ser Cys Lys Gly Phe Phe
50 55 60

Lys Arg Thr Val Gln Asn Asn Lys Arg Tyr Thr Cys Ile Glu Asn Gln
 65 70 75 80

Asn Cys Gln Ile Asp Lys Thr Gln Arg Lys Arg Cys Pro Tyr Cys Arg
 85 90 95

Phe Gln Lys Cys Leu Ser Val Gly Met Lys Leu Glu Ala Val Arg Ala
 100 105 110

Asp Arg Met Arg Gly Gly Arg Asn Lys Phe Gly Pro Met Tyr Lys Arg
 115 120 125

Asp Arg Ala Leu Lys Gln Gln Lys Lys Ala Leu Ile Arg Ala Asn Gly
 130 135 140

Leu Lys Leu Glu Ala Met Ser Gln Val Ile Gln Ala Met Pro Ser Asp
 145 150 155 160

Leu Thr Ile Ser Ser Ala Ile Gln Asn Ile His Ser Ala Ser Lys Gly
 165 170 175

Leu Pro Leu Asn His Ala Ala Leu Pro Pro Thr Asp Tyr Asp Arg Ser
 180 185 190

Pro Phe Val Thr Ser Pro Ile Ser Met Thr Met Pro Pro His Gly Ser
 195 200 205

Leu Gln Gly Tyr Gln Thr Tyr Gly His Phe Pro Ser Arg Ala Ile Lys
 210 215 220

Ser Glu Tyr Pro Asp Pro Tyr Thr Ser Ser Pro Glu Ser Ile Met Gly
 225 230 235 240

Tyr Ser Tyr Met Asp Ser Tyr Gln Thr Ser Ser Pro Ala Ser Ile Pro
 245 250 255

His Leu Ile Leu Glu Leu Leu Lys Cys Glu Pro Asp Glu Pro Gln Val
 260 265 270

Gln Ala Lys Ile Met Ala Tyr Leu Gln Gln Glu Gln Ala Asn Arg Ser
 275 280 285

Lys His Glu Lys Leu Ser Thr Phe Gly Leu Met Cys Lys Met Ala Asp

290 295 300
 Gln Thr Leu Phe Ser Ile Val Glu Trp Ala Arg Ser Ser Ile Phe Phe
 305 310 315 320
 Arg Glu Leu Lys Val Asp Asp Gln Met Lys Leu Leu Gln Asn Cys Trp
 325 330 335
 Ser Glu Leu Leu Ile Leu Asp His Ile Tyr Arg Gln Val Val His Gly
 340 345 350
 Lys Glu Gly Ser Ile Phe Leu Val Thr Gly Gln Gln Val Asp Tyr Ser
 355 360 365
 Ile Ile Ala Ser Gln Ala Gly Ala Thr Leu Asn Asn Leu Met Ser His
 370 375 380
 Ala Gln Glu Leu Val Ala Lys Leu Arg Ser Leu Gln Phe Asp Gln Arg
 385 390 395 400
 Glu Phe Val Cys Leu Lys Phe Leu Val Leu Phe Ser Leu Asp Val Lys
 405 410 415
 Asn Leu Glu Asn Phe Gln Leu Val Glu Gly Val Gln Glu Gln Val Asn
 420 425 430
 Ala Ala Leu Leu Asp Tyr Thr Met Cys Asn Tyr Pro Gln Gln Thr Glu
 435 440 445
 Lys Phe Gly Gln Leu Leu Leu Arg Leu Pro Glu Ile Arg Ala Ile Ser
 450 455 460
 Met Gln Ala Glu Glu Tyr Leu Tyr Tyr Lys His Leu Asn Gly Asp Val
 465 470 475 480
 Pro Tyr Asn Asn Leu Leu Ile Glu Met Leu His Ala Lys Arg Ala
 485 490 495

 <210> 157
 <211> 2303
 <212> PRT
 <213> Human

 <400> 157

 Met Thr Ser Glu Glu Met Thr Ala Ser Val Leu Ile Pro Val Thr Gln

393/439

Ala Lys Asn Cys Asp Asn Lys Asn Glu Gln Leu Gln Cys Asp His Cys
 245 250 255

Asp Thr Leu Asn Asp Lys Tyr Phe Cys Phe Glu Gly Ser Cys Glu Lys
 260 265 270

Val Asp Met Val Tyr Ser Gly Asp Ser Phe Cys Arg Lys Asp Phe Thr
 275 280 285

Asp Ser Gln Ala Ala Lys Thr Phe Leu Ser His Phe Glu Asp Phe Pro
 290 295 300

Asp Asn Cys Asp Asp Val Glu Glu Asp Ala Phe Lys Ser Lys Lys Glu
 305 310 315 320

Arg Ser Thr Leu Leu Val Arg Arg Phe Cys Lys Asn Asp Arg Glu Val
 325 330 335

Lys Lys Ser Val Tyr Thr Gly Thr Arg Ala Ile Val Arg Thr Leu Pro
 340 345 350

Ser Gly His Ile Gly Leu Thr Ala Trp Ser Tyr Ile Asp Gln Lys Arg
 355 360 365

Asn Gly Pro Leu Leu Pro Cys Gly Arg Val Met Glu Pro Pro Ser Thr
 370 375 380

Val Glu Ile Arg Gln Asp Gly Ser Gln Arg Leu Ser Glu Ala Gln Trp
 385 390 395 400

Tyr Pro Ile Tyr Asn Ala Val Arg Arg Glu Glu Thr Glu Asn Thr Val
 405 410 415

Gly Ser Leu Leu His Phe Leu Thr Lys Leu Pro Ala Ser Glu Thr Ala
 420 425 430

His Gly Arg Ile Ser Val Gly Pro Cys Leu Lys Gln Cys Val Arg Asp
 435 440 445

Thr Val Cys Glu Tyr Arg Ala Thr Leu Gln Arg Thr Ser Ile Ser Gln
 450 455 460

Tyr Ile Thr Gly Ser Leu Leu Glu Ala Thr Thr Ser Leu Gly Ala Arg
 465 470 475 480

Ser Gly Leu Leu Ser Thr Phe Gly Gly Ser Thr Gly Arg Met Met Leu
 485 490 495

Lys Glu Arg Gln Pro Gly Pro Ser Val Ala Asn Ser Asn Ala Leu Pro
 500 505 510

Ser Ser Ser Ala Gly Ile Ser Lys Glu Leu Ile Asp Leu Gln Pro Leu
 515 520 525

Ile Gln Phe Pro Glu Glu Val Ala Ser Ile Leu Met Glu Gln Glu Gln
 530 535 540

Thr Ile Tyr Arg Arg Val Leu Pro Val Asp Tyr Leu Cys Phe Leu Thr
 545 550 555 560

Arg Asp Leu Gly Thr Pro Glu Cys Gln Ser Ser Leu Pro Cys Leu Lys
 565 570 575

Ala Ser Ile Ser Ala Ser Ile Leu Thr Thr Gln Asn Gly Glu His Asn
 580 585 590

Ala Leu Glu Asp Leu Val Met Arg Phe Asn Glu Val Ser Ser Trp Val
 595 600 605

Thr Trp Leu Ile Leu Thr Ala Gly Ser Met Glu Glu Lys Arg Glu Val
 610 615 620

Phe Ser Tyr Leu Val His Val Ala Lys Cys Cys Trp Asn Met Gly Asn
 625 630 635 640

Tyr Asn Ala Val Met Glu Phe Leu Ala Gly Leu Arg Ser Arg Lys Val
 645 650 655

Leu Lys Met Trp Gln Phe Met Asp Gln Ser Asp Ile Glu Thr Met Arg
 660 665 670

Ser Leu Lys Asp Ala Met Ala Gln His Glu Ser Ser Cys Glu Tyr Arg
 675 680 685

Lys Val Val Thr Arg Ala Leu His Ile Pro Gly Cys Lys Val Val Pro
 690 695 700

Phe Cys Gly Val Phe Leu Lys Glu Leu Cys Glu Val' Leu Asp Gly Ala
 705 710 715 720

Ser Gly Leu Met Lys Leu Cys Pro Arg Tyr Asn Ser Gln Glu Glu Thr
 725 730 735

Leu Glu Phe Val Ala Asp Tyr Ser Gly Gln Asp Asn Phe Leu Gln Arg
 740 745 750

Val Gly Gln Asn Gly Leu Lys Asn Ser Glu Lys Glu Ser Thr Val Asn
 755 760 765

Ser Ile Phe Gln Val Ile Arg Ser Cys Asn Arg Ser Leu Glu Thr Asp
 770 775 780

Glu Glu Asp Ser Pro Ser Glu Gly Asn Ser Ser Arg Lys Ser Ser Leu
 785 790 795 800

Lys Asp Lys Ser Arg Trp Gln Phe Ile Ile Gly Asp Leu Leu Asp Ser
 805 810 815

Asp Asn Asp Ile Phe Glu Gln Ser Lys Glu Tyr Asp Ser His Gly Ser
 820 825 830

Glu Asp Ser Gln Lys Ala Phe Asp His Gly Thr Glu Leu Ile Pro Trp
 835 840 845

Tyr Val Leu Ser Ile Gln Ala Asp Val His Gln Phe Leu Leu Gln Gly
 850 855 860

Ala Thr Val Ile His Tyr Asp Gln Asp Thr His Leu Ser Ala Arg Cys
 865 870 875 880

Phe Leu Gln Leu Gln Pro Asp Asn Ser Thr Leu Thr Trp Val Lys Pro
 885 890 895

Thr Thr Ala Ser Pro Ala Ser Ser Lys Ala Lys Leu Gly Val Leu Asn
 900 905 910

Asn Thr Ala Glu Pro Gly Lys Phe Pro Leu Leu Gly Asn Ala Gly Leu
 915 920 925

Ser Ser Leu Thr Glu Gly Val Leu Asp Leu Phe Ala Val Lys Ala Val
 930 935 940

Tyr Met Gly His Pro Gly Ile Asp Ile His Thr Val Cys Val Gln Asn

945 950 955 960
 Lys Leu Gly Ser Met Phe Leu Ser Glu Thr Gly Val Thr Leu Leu Tyr
 965 970 975
 Gly Leu Gln Thr Thr Asp Asn Arg Leu Leu His Phe Val Ala Pro Lys
 980 985 990
 His Thr Ala Lys Met Leu Phe Ser Gly Leu Leu Glu Leu Thr Arg Ala
 995 1000 1005
 Val Arg Lys Met Arg Lys Phe Pro Asp Gln Arg Gln Gln Trp Leu
 1010 1015 1020
 Arg Lys Gln Tyr Val Ser Leu Tyr Gln Glu Asp Gly Arg Tyr Glu
 1025 1030 1035
 Gly Pro Thr Leu Ala His Ala Val Glu Leu Phe Gly Gly Arg Arg
 1040 1045 1050
 Trp Ser Ala Arg Asn Pro Ser Pro Gly Thr Ser Ala Lys Asn Ala
 1055 1060 1065
 Glu Lys Pro Asn Met Gln Arg Asn Asn Thr Leu Gly Ile Ser Thr
 1070 1075 1080
 Thr Lys Lys Lys Lys Lys Ile Leu Met Arg Gly Glu Ser Gly Glu
 1085 1090 1095
 Val Thr Asp Asp Glu Met Ala Thr Arg Lys Ala Lys Met His Lys
 1100 1105 1110
 Glu Cys Arg Ser Arg Ser Gly Ser Asp Pro Gln Asp Ile Asn Glu
 1115 1120 1125
 Gln Glu Glu Ser Glu Val Asn Ala Ile Ala Asn Pro Pro Asn Pro
 1130 1135 1140
 Leu Pro Ser Arg Arg Ala His Ser Leu Thr Thr Ala Gly Ser Pro
 1145 1150 1155
 Asn Leu Ala Ala Gly Thr Ser Ser Pro Ile Arg Pro Val Ser Ser
 1160 1165 1170

Pro Val Leu Ser Ser Ser Asn Lys Ser Pro Ser Ser Ala Trp Ser
 1175 1180 1185

 Ser Ser Ser Trp His Gly Arg Ile Lys Gly Gly Met Lys Gly Phe
 1190 1195 1200

 Gln Ser Phe Met Val Ser Asp Ser Asn Met Ser Phe Val Glu Phe
 1205 1210 1215

 Val Glu Leu Phe Lys Ser Phe Ser Val Arg Ser Arg Lys Asp Leu
 1220 1225 1230

 Lys Asp Leu Phe Asp Val Tyr Ala Val Pro Cys Asn Arg Ser Gly
 1235 1240 1245

 Ser Glu Ser Ala Pro Leu Tyr Thr Asn Leu Thr Ile Asp Glu Asn
 1250 1255 1260

 Thr Ser Asp Leu Gln Pro Asp Leu Asp Leu Leu Thr Arg Asn Val
 1265 1270 1275

 Ser Asp Leu Gly Leu Phe Ile Lys Ser Lys Gln Gln Leu Ser Asp
 1280 1285 1290

 Asn Gln Arg Gln Ile Ser Asp Ala Ile Ala Ala Ala Ser Ile Val
 1295 1300 1305

 Thr Asn Gly Thr Gly Ile Glu Ser Thr Ser Leu Gly Ile Phe Gly
 1310 1315 1320

 Val Gly Ile Leu Gln Leu Asn Asp Phe Leu Val Asn Cys Gln Gly
 1325 1330 1335

 Glu His Cys Thr Tyr Asp Glu Ile Leu Ser Ile Ile Gln Lys Phe
 1340 1345 1350

 Glu Pro Ser Ile Ser Met Cys His Gln Gly Leu Met Ser Phe Glu
 1355 1360 1365

 Gly Phe Ala Arg Phe Leu Met Asp Lys Glu Asn Phe Ala Ser Lys
 1370 1375 1380

 Asn Asp Glu Ser Gln Glu Asn Ile Lys Glu Leu Gln Leu Pro Leu
 1385 1390 1395

Ser Tyr Tyr Tyr Ile Glu Ser Ser His Asn Thr Tyr Leu Thr Gly
 1400 1405 1410
 His Gln Leu Lys Gly Glu Ser Ser Val Glu Leu Tyr Ser Gln Val
 1415 1420 1425
 Leu Leu Gln Gly Cys Arg Ser Val Glu Leu Asp Cys Trp Asp Gly
 1430 1435 1440
 Asp Asp Gly Met Pro Ile Ile Tyr His Gly His Thr Pro Thr Thr
 1445 1450 1455
 Lys Ile Pro Phe Lys Glu Val Val Glu Ala Ile Asp Arg Ser Ala
 1460 1465 1470
 Phe Ile Asn Ser Asp Leu Pro Ile Ile Ile Ser Ile Glu Asn His
 1475 1480 1485
 Cys Ser Leu Pro Gln Gln Arg Lys Met Ala Glu Ile Phe Lys Thr
 1490 1495 1500
 Val Phe Gly Glu Lys Leu Val Thr Lys Phe Leu Phe Glu Thr Asp
 1505 1510 1515
 Phe Ser Asp Asp Pro Met Leu Pro Ser Pro Asp Gln Leu Arg Lys
 1520 1525 1530
 Lys Val Leu Leu Lys Asn Lys Lys Leu Lys Ala His Gln Thr Pro
 1535 1540 1545
 Val Asp Ile Leu Lys Gln Lys Ala His Gln Leu Ala Ser Met Gln
 1550 1555 1560
 Val Gln Ala Tyr Asn Gly Gly Asn Ala Asn Pro Arg Pro Ala Asn
 1565 1570 1575
 Asn Glu Glu Glu Glu Asp Glu Glu Asp Glu Tyr Asp Tyr Asp Tyr
 1580 1585 1590
 Glu Ser Leu Ser Asp Asp Asn Ile Leu Glu Asp Arg Pro Glu Asn
 1595 1600 1605
 Lys Ser Cys Asn Asp Lys Leu Gln Phe Glu Tyr Asn Glu Glu Ile
 1610 1615 1620

Pro Lys Arg Ile Lys Lys Ala Asp Asn Ser Ala Cys Asn Lys Gly
 1625 1630 1635
 Lys Val Tyr Asp Met Glu Leu Gly Glu Glu Phe Tyr Leu Asp Gln
 1640 1645 1650
 Asn Lys Lys Glu Ser Arg Gln Ile Ala Pro Glu Leu Ser Asp Leu
 1655 1660 1665
 Val Ile Tyr Arg Gln Ala Val Lys Phe Pro Gly Leu Ser Thr Leu
 1670 1675 1680
 Asn Ala Ser Gly Ser Ser Arg Gly Lys Glu Arg Lys Ser Arg Lys
 1685 1690 1695
 Ser Ile Phe Gly Asn Asn Pro Gly Arg Met Ser Pro Gly Glu Thr
 1700 1705 1710
 Ala Ser Phe Asn Lys Thr Ser Gly Lys Ser Ser Cys Glu Gly Ile
 1715 1720 1725
 Arg Gln Thr Trp Glu Glu Ser Ser Ser Pro Leu Asn Pro Thr Thr
 1730 1735 1740
 Ser Leu Ser Ala Ile Ile Arg Thr Pro Lys Cys Tyr His Ile Ser
 1745 1750 1755
 Ser Leu Asn Glu Asn Ala Ala Lys Arg Leu Cys Arg Arg Tyr Ser
 1760 1765 1770
 Gln Lys Leu Ile Gln His Thr Ala Cys Gln Leu Leu Arg Thr Tyr
 1775 1780 1785
 Pro Ala Ala Thr Arg Ile Asp Ser Ser Asn Pro Asn Pro Leu Met
 1790 1795 1800
 Phe Trp Leu His Gly Ile Gln Leu Val Ala Leu Asn Tyr Gln Thr
 1805 1810 1815
 Asp Asp Leu Pro Leu His Leu Asn Ala Ala Met Phe Glu Ala Asn
 1820 1825 1830
 Gly Gly Cys Gly Tyr Val Leu Lys Pro Pro Val Leu Trp Asp Lys

1835		1840		1845	
Asn Cys Pro Met Tyr Gln Lys Phe Ser Pro Leu Glu Arg Asp Leu					
1850		1855		1860	
Asp Ser Met Asp Pro Ala Val Tyr Ser Leu Thr Ile Val Ser Gly					
1865		1870		1875	
Gln Asn Val Cys Pro Ser Asn Ser Met Gly Ser Pro Cys Ile Glu					
1880		1885		1890	
Val Asp Val Leu Gly Met Pro Leu Asp Ser Cys His Phe Arg Thr					
1895		1900		1905	
Lys Pro Ile His Arg Asn Thr Leu Asn Pro Met Trp Asn Glu Gln					
1910		1915		1920	
Phe Leu Phe Arg Val His Phe Glu Asp Leu Val Phe Leu Arg Phe					
1925		1930		1935	
Ala Val Val Glu Asn Asn Ser Ser Ala Val Thr Ala Gln Arg Ile					
1940		1945		1950	
Ile Pro Leu Lys Ala Leu Lys Arg Gly Tyr Arg His Leu Gln Leu					
1955		1960		1965	
Arg Asn Leu His Asn Glu Val Leu Glu Ile Ser Ser Leu Phe Ile					
1970		1975		1980	
Asn Ser Arg Arg Met Glu Glu Asn Ser Ser Gly Asn Thr Met Ser					
1985		1990		1995	
Ala Ser Ser Met Phe Asn Thr Glu Glu Arg Lys Cys Leu Gln Thr					
2000		2005		2010	
His Arg Val Thr Val His Gly Val Pro Gly Pro Glu Pro Phe Thr					
2015		2020		2025	
Val Phe Thr Ile Asn Gly Gly Thr Lys Ala Lys Gln Leu Leu Gln					
2030		2035		2040	
Gln Ile Leu Thr Asn Glu Gln Asp Ile Lys Pro Val Thr Thr Asp					
2045		2050		2055	

Tyr Phe	Leu Met	Glu Glu	Lys	Tyr Phe	Ile Ser	Lys	Glu Lys	Asn
2060			2065			2070		
Glu Cys	Arg Lys	Gln Pro	Phe	Gln Arg	Ala Ile	Gly	Pro Glu	Glu
2075			2080			2085		
Glu Ile	Met Gln	Ile Leu	Ser	Ser Trp	Phe Pro	Glu	Glu Gly	Tyr
2090			2095			2100		
Met Gly	Arg Ile	Val Leu	Lys	Thr Gln	Gln Glu	Asn	Leu Glu	Glu
2105			2110			2115		
Lys Asn	Ile Val	Gln Asp	Asp	Lys Glu	Val Ile	Leu	Ser Ser	Glu
2120			2125			2130		
Glu Glu	Ser Phe	Phe Val	Gln	Val His	Asp Val	Ser	Pro Glu	Gln
2135			2140			2145		
Pro Arg	Thr Val	Ile Lys	Ala	Pro Arg	Val Ser	Thr	Ala Gln	Asp
2150			2155			2160		
Val Ile	Gln Gln	Thr Leu	Cys	Lys Ala	Lys Tyr	Ser	Tyr Ser	Ile
2165			2170			2175		
Leu Ser	Asn Pro	Asn Pro	Ser	Asp Tyr	Val Leu	Leu	Glu Glu	Val
2180			2185			2190		
Val Lys	Asp Thr	Thr Asn	Lys	Lys Thr	Thr Thr	Pro	Lys Ser	Ser
2195			2200			2205		
Gln Arg	Val Leu	Leu Asp	Gln	Glu Cys	Val Phe	Gln	Ala Gln	Ser
2210			2215			2220		
Lys Trp	Lys Gly	Ala Gly	Lys	Phe Ile	Leu Lys	Leu	Lys Glu	Gln
2225			2230			2235		
Val Gln	Ala Ser	Arg Glu	Asp	Lys Lys	Lys Gly	Ile	Ser Phe	Ala
2240			2245			2250		
Ser Glu	Leu Lys	Lys Leu	Thr	Lys Ser	Thr Lys	Gln	Pro Arg	Gly
2255			2260			2265		
Leu Thr	Ser Pro	Ser Gln	Leu	Leu Thr	Ser Glu	Ser	Ile Gln	Thr
2270			2275			2280		

Lys Glu Glu Lys Pro Val Gly Gly Leu Ser Pro Val Thr Gln Trp
 2285 2290 2295

Ile Thr Asp Ser Asp
 2300

<210> 158
 <211> 303
 <212> PRT
 <213> Human

<400> 158

Met Ala Ser Trp Ala Lys Gly Arg Ser Tyr Leu Ala Pro Gly Leu Leu
 1 5 10 15

Gln Gly Gln Val Ala Ile Val Thr Gly Gly Ala Thr Gly Ile Gly Lys
 20 25 30

Ala Ile Val Lys Glu Leu Leu Glu Leu Gly Ser Asn Val Val Ile Ala
 35 40 45

Ser Arg Lys Leu Glu Arg Leu Lys Ser Ala Ala Asp Glu Leu Gln Ala
 50 55 60

Asn Leu Pro Pro Thr Lys Gln Ala Arg Val Ile Pro Ile Gln Cys Asn
 65 70 75 80

Ile Arg Asn Glu Glu Glu Val Asn Asn Leu Val Lys Ser Thr Leu Asp
 85 90 95

Thr Phe Gly Lys Ile Asn Phe Leu Val Asn Asn Gly Gly Gly Gln Phe
 100 105 110

Leu Ser Pro Ala Glu His Ile Ser Ser Lys Gly Trp His Ala Val Leu
 115 120 125

Glu Thr Asn Leu Thr Gly Thr Phe Tyr Met Cys Lys Ala Val Tyr Ser
 130 135 140

Ser Trp Met Lys Glu His Gly Gly Ser Ile Val Asn Ile Ile Val Pro
 145 150 155 160

Thr Lys Ala Gly Phe Pro Leu Ala Val His Ser Gly Ala Ala Arg Ala
 165 170 175

Gly Val Tyr Asn Leu Thr Lys Ser Leu Ala Leu Glu Trp Ala Cys Ser
 180 185 190

Gly Ile Arg Ile Asn Cys Val Ala Pro Gly Val Ile Tyr Ser Gln Thr
 195 200 205

Ala Val Glu Asn Tyr Gly Ser Trp Gly Gln Ser Phe Phe Glu Gly Ser
 210 215 220

Phe Gln Lys Ile Pro Ala Lys Arg Ile Gly Val Pro Glu Glu Val Ser
 225 230 235 240

Ser Val Val Cys Phe Leu Leu Ser Pro Ala Ala Ser Phe Ile Thr Gly
 245 250 255

Gln Ser Val Asp Val Asp Gly Gly Arg Ser Leu Tyr Thr His Ser Tyr
 260 265 270

Glu Val Pro Asp His Asp Asn Trp Pro Lys Gly Ala Gly Asp Leu Ser
 275 280 285

Val Val Lys Lys Met Lys Glu Thr Phe Lys Glu Lys Ala Lys Leu
 290 295 300

<210> 159
 <211> 246
 <212> PRT
 <213> Human

<400> 159

Met Glu Glu Ala Lys Ser Gln Ser Leu Glu Glu Asp Phe Glu Gly Gln
 1 5 10 15

Ala Thr His Thr Gly Pro Lys Gly Val Ile Asn Asp Trp Arg Lys Phe
 20 25 30

Lys Leu Glu Ser Gln Asp Ser Asp Ser Ile Pro Pro Ser Lys Lys Glu
 35 40 45

Ile Leu Arg Gln Met Ser Ser Pro Gln Ser Arg Asn Gly Lys Asp Ser
 50 55 60

Lys Glu Arg Val Ser Arg Lys Met Ser Ile Gln Glu Tyr Glu Leu Ile
 65 70 75 80

His Lys Glu Lys Glu Asp Glu Asn Cys Leu Arg Lys Tyr Arg Arg Gln
 85 90 95

Cys Met Gln Asp Met His Gln Lys Leu Ser Phe Gly Pro Arg Tyr Gly
 100 105 110

Phe Val Tyr Glu Leu Glu Thr Gly Lys Gln Phe Leu Glu Thr Ile Glu
 115 120 125

Lys Glu Leu Lys Ile Thr Thr Ile Val Val His Ile Tyr Glu Asp Gly
 130 135 140

Ile Lys Gly Cys Asp Ala Leu Asn Ser Ser Leu Thr Cys Leu Ala Ala
 145 150 155 160

Glu Tyr Pro Ile Val Lys Phe Cys Lys Ile Lys Ala Ser Asn Thr Gly
 165 170 175

Ala Gly Asp Arg Phe Ser Leu Asp Val Leu Pro Thr Leu Leu Ile Tyr
 180 185 190

Lys Gly Gly Glu Leu Ile Ser Asn Phe Ile Ser Val Ala Glu Gln Phe
 195 200 205

Ala Glu Glu Phe Phe Ala Gly Asp Val Glu Ser Phe Leu Asn Glu Tyr
 210 215 220

Gly Leu Leu Pro Glu Arg Glu Val His Val Leu Glu His Thr Lys Ile
 225 230 235 240

Glu Glu Glu Asp Val Glu
 245

<210> 160
 <211> 403
 <212> PRT
 <213> Human

<400> 160

Met Thr Ala Ile Ile Lys Glu Ile Val Ser Arg Asn Lys Arg Arg Tyr
 1 5 10 15

Gln Glu Asp Gly Phe Asp Leu Asp Leu Thr Tyr Ile Tyr Pro Asn Ile
 20 25 30

Ile Ala Met Gly Phe Pro Ala Glu Arg Leu Glu Gly Val Tyr Arg Asn
 35 40 45
 Asn Ile Asp Asp Val Val Arg Phe Leu Asp Ser Lys His Lys Asn His
 50 55 60
 Tyr Lys Ile Tyr Asn Leu Cys Ala Glu Arg His Tyr Asp Thr Ala Lys
 65 70 75 80
 Phe Asn Cys Arg Val Ala Gln Tyr Pro Phe Glu Asp His Asn Pro Pro
 85 90 95
 Gln Leu Glu Leu Ile Lys Pro Phe Cys Glu Asp Leu Asp Gln Trp Leu
 100 105 110
 Ser Glu Asp Asp Asn His Val Ala Ala Ile His Cys Lys Ala Gly Lys
 115 120 125
 Gly Arg Thr Gly Val Met Ile Cys Ala Tyr Leu Leu His Arg Gly Lys
 130 135 140
 Phe Leu Lys Ala Gln Glu Ala Leu Asp Phe Tyr Gly Glu Val Arg Thr
 145 150 155 160
 Arg Asp Lys Lys Gly Val Thr Ile Pro Ser Gln Arg Arg Tyr Val Tyr
 165 170 175
 Tyr Tyr Ser Tyr Leu Leu Lys Asn His Leu Asp Tyr Arg Pro Val Ala
 180 185 190
 Leu Leu Phe His Lys Met Met Phe Glu Thr Ile Pro Met Phe Ser Gly
 195 200 205
 Gly Thr Cys Asn Pro Gln Phe Val Val Cys Gln Leu Lys Val Lys Ile
 210 215 220
 Tyr Ser Ser Asn Ser Gly Pro Thr Arg Arg Glu Asp Lys Phe Met Tyr
 225 230 235 240
 Phe Glu Phe Pro Gln Pro Leu Pro Val Cys Gly Asp Ile Lys Val Glu
 245 250 255
 Phe Phe His Lys Gln Asn Lys Met Leu Lys Lys Asp Lys Met Phe His
 260 265 270

Phe Trp Val Asn Thr Phe Phe Ile Pro Gly Pro Glu Glu Thr Ser Glu
 275 280 285

Lys Val Glu Asn Gly Ser Leu Cys Asp Gln Glu Ile Asp Ser Ile Cys
 290 295 300

Ser Ile Glu Arg Ala Asp Asn Asp Lys Glu Tyr Leu Val Leu Thr Leu
 305 310 315 320

Thr Lys Asn Asp Leu Asp Lys Ala Asn Lys Asp Lys Ala Asn Arg Tyr
 325 330 335

Phe Ser Pro Asn Phe Lys Val Lys Leu Tyr Phe Thr Lys Thr Val Glu
 340 345 350

Glu Pro Ser Asn Pro Glu Ala Ser Ser Ser Thr Ser Val Thr Pro Asp
 355 360 365

Val Ser Asp Asn Glu Pro Asp His Tyr Arg Tyr Ser Asp Thr Thr Asp
 370 375 380

Ser Asp Pro Glu Asn Glu Pro Phe Asp Glu Asp Gln His Thr Gln Ile
 385 390 395 400

Thr Lys Val

<210> 161
 <211> 336
 <212> PRT
 <213> Human

<400> 161

Met Leu Gln Ser Leu Ala Gly Ser Ser Cys Val Arg Leu Val Glu Arg
 1 5 10 15

His Arg Ser Ala Trp Cys Phe Gly Phe Leu Val Leu Gly Tyr Leu Leu
 20 25 30

Tyr Leu Val Phe Gly Ala Val Val Phe Ser Ser Val Glu Leu Pro Tyr
 35 40 45

Glu Asp Leu Leu Arg Gln Glu Leu Arg Lys Leu Lys Arg Arg Phe Leu
 50 55 60

Glu Glu His Glu Cys Leu Ser Glu Gln Gln Leu Glu Gln Phe Leu Gly
65 70 75 80

Arg Val Leu Glu Ala Ser Asn Tyr Gly Val Ser Val Leu Ser Asn Ala
85 90 95

Ser Gly Asn Trp Asn Trp Asp Phe Thr Ser Ala Leu Phe Phe Ala Ser
100 105 110

Thr Val Leu Ser Thr Thr Gly Tyr Gly His Thr Val Pro Leu Ser Asp
115 120 125

Gly Gly Lys Ala Phe Cys Ile Ile Tyr Ser Val Ile Gly Ile Pro Phe
130 135 140

Thr Leu Leu Phe Leu Thr Ala Val Val Gln Arg Ile Thr Val His Val
145 150 155 160

Thr Arg Arg Pro Val Leu Tyr Phe His Ile Arg Trp Gly Phe Ser Lys
165 170 175

Gln Val Val Ala Ile Val His Ala Val Leu Leu Gly Phe Val Thr Val
180 185 190

Ser Cys Phe Phe Phe Ile Pro Ala Ala Val Phe Ser Val Leu Glu Asp
195 200 205

Asp Trp Asn Phe Leu Glu Ser Phe Tyr Phe Cys Phe Ile Ser Leu Ser
210 215 220

Thr Ile Gly Leu Gly Asp Tyr Val Pro Gly Glu Gly Tyr Asn Gln Lys
225 230 235 240

Phe Arg Glu Leu Tyr Lys Ile Gly Ile Thr Cys Tyr Leu Leu Leu Gly
245 250 255

Leu Ile Ala Met Leu Val Val Leu Glu Thr Phe Cys Glu Leu His Glu
260 265 270

Leu Lys Lys Phe Arg Lys Met Phe Tyr Val Lys Lys Asp Lys Asp Glu
275 280 285

Asp Gln Val His Ile Ile Glu His Asp Gln Leu Ser Phe Ser Ser Ile

290 295 300
 Thr Asp Gln Ala Ala Gly Met Lys Glu Asp Gln Lys Gln Asn Glu Pro
 305 310 315 320

 Phe Val Ala Thr Gln Ser Ser Ala Cys Val Asp Gly Pro Ala Asn His
 325 330 335

 <210> 162
 <211> 604
 <212> PRT
 <213> Human

 <400> 162
 Met Leu Ala Arg Ala Leu Leu Leu Cys Ala Val Leu Ala Leu Ser His
 1 5 10 15

 Thr Ala Asn Pro Cys Cys Ser His Pro Cys Gln Asn Arg Gly Val Cys
 20 25 30

 Met Ser Val Gly Phe Asp Gln Tyr Lys Cys Asp Cys Thr Arg Thr Gly
 35 40 45

 Phe Tyr Gly Glu Asn Cys Ser Thr Pro Glu Phe Leu Thr Arg Ile Lys
 50 55 60

 Leu Phe Leu Lys Pro Thr Pro Asn Thr Val His Tyr Ile Leu Thr His
 65 70 75 80

 Phe Lys Gly Phe Trp Asn Val Val Asn Asn Ile Pro Phe Leu Arg Asn
 85 90 95

 Ala Ile Met Ser Tyr Val Leu Thr Ser Arg Ser His Leu Ile Asp Ser
 100 105 110

 Pro Pro Thr Tyr Asn Ala Asp Tyr Gly Tyr Lys Ser Trp Glu Ala Phe
 115 120 125

 Ser Asn Leu Ser Tyr Tyr Thr Arg Ala Leu Pro Pro Val Pro Asp Asp
 130 135 140

 Cys Pro Thr Pro Leu Gly Val Lys Gly Lys Lys Gln Leu Pro Asp Ser
 145 150 155 160

 Asn Glu Ile Val Glu Lys Leu Leu Leu Arg Arg Lys Phe Ile Pro Asp

165	170	175
Pro Gln Gly Ser Asn Met Met Phe Ala Phe Phe Ala Gln His Phe Thr		
180	185	190
His Gln Phe Phe Lys Thr Asp His Lys Arg Gly Pro Ala Phe Thr Asn		
195	200	205
Gly Leu Gly His Gly Val Asp Leu Asn His Ile Tyr Gly Glu Thr Leu		
210	215	220
Ala Arg Gln Arg Lys Leu Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr		
225	230	235 240
Gln Ile Ile Asp Gly Glu Met Tyr Pro Pro Thr Val Lys Asp Thr Gln		
245	250	255
Ala Glu Met Ile Tyr Pro Pro Gln Val Pro Glu His Leu Arg Phe Ala		
260	265	270
Val Gly Gln Glu Val Phe Gly Leu Val Pro Gly Leu Met Met Tyr Ala		
275	280	285
Thr Ile Trp Leu Arg Glu His Asn Arg Val Cys Asp Val Leu Lys Gln		
290	295	300
Glu His Pro Glu Trp Gly Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu		
305	310	315 320
Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Asp Tyr Val Gln		
325	330	335
His Leu Ser Gly Tyr His Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu		
340	345	350
Phe Asn Lys Gln Phe Gln Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn		
355	360	365
Thr Leu Tyr His Trp His Pro Leu Leu Pro Asp Thr Phe Gln Ile His		
370	375	380
Asp Gln Lys Tyr Asn Tyr Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu		
385	390	395 400

Leu Glu His Gly Ile Thr Gln Phe Val Glu Ser Phe Thr Arg Gln Ile
 405 410 415

Ala Gly Arg Val Ala Gly Gly Arg Asn Val Pro Pro Ala Val Gln Lys
 420 425 430

Val Ser Gln Ala Ser Ile Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser
 435 440 445

Phe Asn Glu Tyr Arg Lys Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe
 450 455 460

Glu Glu Leu Thr Gly Glu Lys Glu Met Ser Ala Glu Leu Glu Ala Leu
 465 470 475 480

Tyr Gly Asp Ile Asp Ala Val Glu Leu Tyr Pro Ala Leu Leu Val Glu
 485 490 495

Lys Pro Arg Pro Asp Ala Ile Phe Gly Glu Thr Met Val Glu Val Gly
 500 505 510

Ala Pro Phe Ser Leu Lys Gly Leu Met Gly Asn Val Ile Cys Ser Pro
 515 520 525

Ala Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Gln Ile
 530 535 540

Ile Asn Thr Ala Ser Ile Gln Ser Leu Ile Cys Asn Asn Val Lys Gly
 545 550 555 560

Cys Pro Phe Thr Ser Phe Ser Val Pro Asp Pro Glu Leu Ile Lys Thr
 565 570 575

Val Thr Ile Asn Ala Ser Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn
 580 585 590

Pro Thr Val Leu Leu Lys Glu Arg Ser Thr Glu Leu
 595 600

<210> 163
 <211> 117
 <212> PRT
 <213> Human
 <400> 163

Met Arg Ala Ser Ser Phe Leu Ile Val Val Phe Leu Ile Ala Gly
1 5 10 15

Thr Leu Val Leu Glu Ala Ala Val Thr Gly Val Pro Val Lys Gly Gln
20 25 30

Asp Thr Val Lys Gly Arg Val Pro Phe Asn Gly Gln Asp Pro Val Lys
35 40 45

Gly Gln Val Ser Val Lys Gly Gln Asp Lys Val Lys Ala Gln Glu Pro
50 55 60

Val Lys Gly Pro Val Ser Thr Lys Pro Gly Ser Cys Pro Ile Ile Leu
65 70 75 80

Ile Arg Cys Ala Met Leu Asn Pro Pro Asn Arg Cys Leu Lys Asp Thr
85 90 95

Asp Cys Pro Gly Ile Lys Lys Cys Cys Glu Gly Ser Cys Gly Met Ala
100 105 110

Cys Phe Val Pro Gln
115

<210> 164
<211> 464
<212> PRT
<213> Human

<400> 164

Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp
1 5 10 15

Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
20 25 30

Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
35 40 45

Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln
50 55 60

Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn
65 70 75 80

Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu
 85 90 95

Phe Asp Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser
 100 105 110

Asn Ser Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp
 115 120 125

Asp Tyr Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro
 130 135 140

Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser
 145 150 155 160

His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu
 165 170 175

His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu
 180 185 190

Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro
 195 200 205

Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe
 210 215 220

Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile
 225 230 235 240

Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu
 245 250 255

Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg
 260 265 270

Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp
 275 280 285

Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg
 290 295 300

Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu
 305 310 315 320

Gly Ile Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln
 325 330 335

Ile Leu Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu
 340 345 350

Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met
 355 360 365

Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro
 370 375 380

Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe
 385 390 395 400

Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu
 405 410 415

Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala
 420 425 430

Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr
 435 440 445

Lys Pro Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu
 450 455 460

<210> 165
 <211> 156
 <212> PRT
 <213> Human

<400> 165

Met Ala Leu Glu Lys Ser Leu Val Arg Leu Leu Leu Val Leu Ile
 1 5 10 15

Leu Leu Val Leu Gly Trp Val Gln Pro Ser Leu Gly Lys Glu Ser Arg
 20 25 30

Ala Lys Lys Phe Gln Arg Gln His Met Asp Ser Asp Ser Ser Pro Ser
 35 40 45

Ser Ser Ser Thr Tyr Cys Asn Gln Met Met Arg Arg Arg Asn Met Thr
 50 55 60

Gln Gly Arg Cys Lys Pro Val Asn Thr Phe Val His Glu Pro Leu Val
65 70 75 80

Asp Val Gln Asn Val Cys Phe Gln Glu Lys Val Thr Cys Lys Asn Gly
85 90 95

Gln Gly Asn Cys Tyr Lys Ser Asn Ser Ser Met His Ile Thr Asp Cys
100 105 110

Arg Leu Thr Asn Gly Ser Arg Tyr Pro Asn Cys Ala Tyr Arg Thr Ser
115 120 125

Pro Lys Glu Arg His Ile Ile Val Ala Cys Glu Gly Ser Pro Tyr Val
130 135 140

Pro Val His Phe Asp Ala Ser Val Glu Asp Ser Thr
145 150 155

<210> 166
<211> 375
<212> PRT
<213> Human

<400> 166

Met Asp Ala Leu Gln Leu Ala Asn Ser Ala Phe Ala Val Asp Leu Phe
1 5 10 15

Lys Gln Leu Cys Glu Lys Glu Pro Leu Gly Asn Val Leu Phe Ser Pro
20 25 30

Ile Cys Leu Ser Thr Ser Leu Ser Leu Ala Gln Val Gly Ala Lys Gly
35 40 45

Asp Thr Ala Asn Glu Ile Gly Gln Val Leu His Phe Glu Asn Val Lys
50 55 60

Asp Ile Pro Phe Gly Phe Gln Thr Val Thr Ser Asp Val Asn Lys Leu
65 70 75 80

Ser Ser Phe Tyr Ser Leu Lys Leu Ile Lys Arg Leu Tyr Val Asp Lys
85 90 95

Ser Leu Asn Leu Ser Thr Glu Phe Ile Ser Ser Thr Lys Arg Pro Tyr
100 105 110

Ala Lys Glu Leu Glu Thr Val Asp Phe Lys Asp Lys Leu Glu Glu Thr
 115 120 125
 Lys Gly Gln Ile Asn Asn Ser Ile Lys Asp Leu Thr Asp Gly His Phe
 130 135 140
 Glu Asn Ile Leu Ala Asp Asn Ser Val Asn Asp Gln Thr Lys Ile Leu
 145 150 155 160
 Val Val Asn Ala Ala Tyr Phe Val Gly Lys Trp Met Lys Lys Phe Pro
 165 170 175
 Glu Ser Glu Thr Lys Glu Cys Pro Phe Arg Leu Asn Lys Thr Asp Thr
 180 185 190
 Lys Pro Val Gln Met Met Asn Met Glu Ala Thr Phe Cys Met Gly Asn
 195 200 205
 Ile Asp Ser Ile Asn Cys Lys Ile Ile Glu Leu Pro Phe Gln Asn Lys
 210 215 220
 His Leu Ser Met Phe Ile Leu Leu Pro Lys Asp Val Glu Asp Glu Ser
 225 230 235 240
 Thr Gly Leu Glu Lys Ile Glu Lys Gln Leu Asn Ser Glu Ser Leu Ser
 245 250 255
 Gln Trp Thr Asn Pro Ser Thr Met Ala Asn Ala Lys Val Lys Leu Ser
 260 265 270
 Ile Pro Lys Phe Lys Val Glu Lys Met Ile Asp Pro Lys Ala Cys Leu
 275 280 285
 Glu Asn Leu Gly Leu Lys His Ile Phe Ser Glu Asp Thr Ser Asp Phe
 290 295 300
 Ser Gly Met Ser Glu Thr Lys Gly Val Ala Leu Ser Asn Val Ile His
 305 310 315 320
 Lys Val Cys Leu Glu Ile Thr Glu Asp Gly Gly Asp Ser Ile Glu Val
 325 330 335
 Pro Gly Ala Arg Ile Leu Gln His Lys Asp Glu Leu Asn Ala Asp His
 340 345 350

Pro Phe Ile Tyr Ile Ile Arg His Asn Lys Thr Arg Asn Ile Ile Phe
 355 360 365

Phe Gly Lys Phe Cys Ser Pro
 370 375

<210> 167
 <211> 240
 <212> PRT
 <213> Human

<400> 167

Met Leu Ala Leu Leu Cys Ser Cys Leu Leu Leu Ala Ala Gly Ala Ser
 1 5 10 15

Asp Ala Trp Thr Gly Glu Asp Ser Ala Glu Pro Asn Ser Asp Ser Ala
 20 25 30

Glu Trp Ile Arg Asp Met Tyr Ala Lys Val Thr Glu Ile Trp Gln Glu
 35 40 45

Val Met Gln Arg Arg Asp Asp Asp Gly Thr Leu His Ala Ala Cys Gln
 50 55 60

Val Gln Pro Ser Ala Thr Leu Asp Ala Ala Gln Pro Arg Val Thr Gly
 65 70 75 80

Val Val Leu Phe Arg Gln Leu Ala Pro Arg Ala Lys Leu Asp Ala Phe
 85 90 95

Phe Ala Leu Glu Gly Phe Pro Thr Glu Pro Asn Ser Ser Ser Arg Ala
 100 105 110

Ile His Val His Gln Phe Gly Asp Leu Ser Gln Gly Cys Glu Ser Thr
 115 120 125

Gly Pro His Tyr Asn Pro Leu Ala Val Pro His Pro Gln His Pro Gly
 130 135 140

Asp Phe Gly Asn Phe Ala Val Arg Asp Gly Ser Leu Trp Arg Tyr Arg
 145 150 155 160

Ala Gly Leu Ala Ala Ser Leu Ala Gly Pro His Ser Ile Val Gly Arg
 165 170 175

...

Ala Val Val Val His Ala Gly Glu Asp Asp Leu Gly Arg Gly Gly Asn
180 185 190

Gln Ala Ser Val Glu Asn Gly Asn Ala Gly Arg Arg Leu Ala Cys Cys
195 200 205

Val Val Gly Val Cys Gly Pro Gly Leu Trp Glu Arg Gln Ala Arg Glu
210 215 220

His Ser Glu Arg Lys Lys Arg Arg Arg Glu Ser Glu Cys Lys Ala Ala
225 230 235 240

<210> 168
<211> 283
<212> PRT
<213> Human

<400> 168

Met Glu Pro Pro Gly Asp Trp Gly Pro Pro Pro Trp Arg Ser Thr Pro
1 5 10 15

Arg Thr Asp Val Leu Arg Leu Val Leu Tyr Leu Thr Phe Leu Gly Ala
20 25 30

Pro Cys Tyr Ala Pro Ala Leu Pro Ser Cys Lys Glu Asp Glu Tyr Pro
35 40 45

Val Gly Ser Glu Cys Cys Pro Lys Cys Ser Pro Gly Tyr Arg Val Lys
50 55 60

Glu Ala Cys Gly Glu Leu Thr Gly Thr Val Cys Glu Pro Cys Pro Pro
65 70 75 80

Gly Thr Tyr Ile Ala His Leu Asn Gly Leu Ser Lys Cys Leu Gln Cys
85 90 95

Gln Met Cys Asp Pro Ala Met Gly Leu Arg Ala Ser Arg Asn Cys Ser
100 105 110

Arg Thr Glu Asn Ala Val Cys Gly Cys Ser Pro Gly His Phe Cys Ile
115 120 125

Val Gln Asp Gly Asp His Cys Ala Ala Cys Arg Ala Tyr Ala Thr Ser
130 135 140

Ser Pro Gly Gln Arg Val Gln Lys Gly Gly Thr Glu Ser Gln Asp Thr
145 150 155 160

Leu Cys Gln Asn Cys Pro Pro Gly Thr Phe Ser Pro Asn Gly Thr Leu
165 170 175

Glu Glu Cys Gln His Gln Thr Lys Cys Ser Trp Leu Val Thr Lys Ala
180 185 190

Gly Ala Gly Thr Ser Ser Ser His Trp Val Trp Trp Phe Leu Ser Gly
195 200 205

Ser Leu Val Ile Val Ile Val Cys Ser Thr Val Gly Leu Ile Ile Cys
210 215 220

Val Lys Arg Arg Lys Pro Arg Gly Asp Val Val Lys Val Ile Val Ser
225 230 235 240

Val Gln Arg Lys Arg Gln Glu Ala Glu Gly Glu Ala Thr Val Ile Glu
245 250 255

Ala Leu Gln Ala Pro Pro Asp Val Thr Thr Val Ala Val Glu Glu Thr
260 265 270

Ile Pro Ser Phe Thr Gly Arg Ser Pro Asn His
275 280

<210> 169
<211> 335
<212> PRT
<213> Human

<400> 169

Met Leu Gly Ile Trp Thr Leu Leu Pro Leu Val Leu Thr Ser Val Ala
1 5 10 15

Arg Leu Ser Ser Lys Ser Val Asn Ala Gln Val Thr Asp Ile Asn Ser
20 25 30

Lys Gly Leu Glu Leu Arg Lys Thr Val Thr Thr Val Glu Thr Gln Asn
35 40 45

Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro
50 55 60

Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro
65 70 75 80

Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His
85 90 95

Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly
100 105 110

Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg
115 120 125

Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp
130 135 140

Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr
145 150 155 160

Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp
165 170 175

Leu Cys Leu Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg
180 185 190

Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly
195 200 205

Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu
210 215 220

Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met
225 230 235 240

Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu
245 250 255

Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu
260 265 270

Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys
275 280 285

Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys

290 295 300
 Thr Leu Ala Glu Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser
 305 310 315 320
 Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val
 325 330 335

 <210> 170
 <211> 207
 <212> PRT
 <213> Human

 <400> 170
 Met Asn Val Ala Arg Phe Leu Val Glu Lys His Thr Leu His Val Ile
 1 5 10 15
 Ile Asp Phe Ile Leu Ser Lys Val Ser Asn Gln Gln Ser Asn Leu Ala
 20 25 30
 Gln His Gln Arg Val Tyr Thr Gly Glu Lys Pro Tyr Lys Cys Asn Glu
 35 40 45
 Trp Gly Lys Ala Leu Ser Gly Lys Ser Ser Leu Phe Tyr His Gln Ala
 50 55 60
 Ile His Gly Val Gly Lys Leu Cys Lys Cys Asn Asp Cys His Lys Val
 65 70 75 80
 Phe Ser Asn Ala Thr Thr Ile Ala Asn His Trp Arg Ile His Asn Glu
 85 90 95
 Asp Arg Ser Tyr Lys Cys Asn Lys Cys Gly Lys Ile Phe Arg His Arg
 100 105 110
 Ser Tyr Leu Ala Val Tyr Gln Arg Thr His Thr Gly Glu Lys Pro Tyr
 115 120 125
 Lys Tyr His Asp Cys Gly Lys Val Phe Ser Gln Ala Ser Ser Tyr Ala
 130 135 140
 Lys His Arg Arg Ile His Thr Gly Glu Lys Pro His Lys Cys Asp Asp
 145 150 155 160
 Cys Gly Lys Val Leu Thr Ser Arg Ser His Leu Ile Arg His Gln Arg

165 170 175
 Ile His Thr Gly Gln Lys Ser Tyr Lys Cys Leu Lys Cys Gly Lys Val
 180 185 190

 Phe Ser Leu Trp Ala Leu His Ala Glu His Gln Lys Ile His Phe
 195 200 205

 <210> 171
 <211> 158
 <212> PRT
 <213> Human

 <400> 171

 Met Ala Ser Arg Ser Met Arg Leu Leu Leu Leu Leu Ser Cys Leu Ala
 1 5 10 15

 Lys Thr Gly Val Leu Gly Asp Ile Ile Met Arg Pro Ser Cys Ala Pro
 20 25 30

 Gly Trp Phe Tyr His Lys Ser Asn Cys Tyr Gly Tyr Phe Arg Lys Leu
 35 40 45

 Arg Asn Trp Ser Asp Ala Glu Leu Glu Cys Gln Ser Tyr Gly Asn Gly
 50 55 60

 Ala His Leu Ala Ser Ile Leu Ser Leu Lys Glu Ala Ser Thr Ile Ala
 65 70 75 80

 Glu Tyr Ile Ser Gly Tyr Gln Arg Ser Gln Pro Ile Trp Ile Gly Leu
 85 90 95

 His Asp Pro Gln Lys Arg Gln Gln Trp Gln Trp Ile Asp Gly Ala Met
 100 105 110

 Tyr Leu Tyr Arg Ser Trp Ser Gly Lys Ser Met Gly Gly Asn Lys His
 115 120 125

 Cys Ala Glu Met Ser Ser Asn Asn Asn Phe Leu Thr Trp Ser Ser Asn
 130 135 140

 Glu Cys Asn Lys Arg Gln His Phe Leu Cys Lys Tyr Arg Pro
 145 150 155

 <210> 172

<211> 432
 <212> PRT
 <213> Human

<400> 172

Met Gly Pro Ala Gly Ser Leu Leu Gly Ser Gly Gln Met Gln Ile Thr
 1 5 10 15

Leu Trp Gly Ser Leu Ala Ala Val Ala Ile Phe Phe Val Ile Thr Phe
 20 25 30

Leu Ile Phe Pro Cys Ser Ser Cys Asp Arg Glu Lys Lys Pro Arg Gln
 35 40 45

His Ser Gly Asp His Glu Asn Leu Met Asn Val Pro Ser Asp Lys Glu
 50 55 60

Met Phe Ser Arg Ser Val Thr Ser Leu Ala Thr Asp Ala Pro Ala Ser
 65 70 75 80

Ser Glu Gln Asn Gly Ala Leu Thr Asn Gly Asp Ile Leu Ser Glu Asp
 85 90 95

Ser Thr Leu Thr Cys Met Gln His Tyr Glu Glu Val Gln Thr Ser Ala
 100 105 110

Ser Asp Leu Leu Asp Ser Gln Asp Ser Thr Gly Lys Pro Lys Cys His
 115 120 125

Gln Ser Arg Glu Leu Pro Arg Ile Pro Pro Glu Ser Ala Val Asp Thr
 130 135 140

Met Leu Thr Ala Arg Ser Val Asp Gly Asp Gln Gly Leu Gly Met Glu
 145 150 155 160

Gly Pro Tyr Glu Val Leu Lys Asp Ser Ser Ser Gln Glu Asn Met Val
 165 170 175

Glu Asp Cys Leu Tyr Glu Thr Val Lys Glu Ile Lys Glu Val Ala Ala
 180 185 190

Ala Ala His Leu Glu Lys Gly His Ser Gly Lys Ala Lys Ser Thr Ser
 195 200 205

Ala Ser Lys Glu Leu Pro Gly Pro Gln Thr Glu Gly Lys Ala Glu Phe

210 215 220
 Ala Glu Tyr Ala Ser Val Asp Arg Asn Lys Lys Cys Arg Gln Ser Val
 225 230 235 240
 Asn Val Glu Ser Ile Leu Gly Asn Ser Cys Asp Pro Glu Glu Glu Ala
 245 250 255
 Pro Pro Pro Val Pro Val Lys Leu Leu Asp Glu Asn Glu Asn Leu Gln
 260 265 270
 Glu Lys Glu Gly Gly Glu Ala Glu Glu Ser Ala Thr Asp Thr Thr Ser
 275 280 285
 Glu Thr Asn Lys Arg Phe Ser Ser Leu Ser Tyr Lys Ser Arg Glu Glu
 290 295 300
 Asp Pro Thr Leu Thr Glu Glu Glu Ile Ser Ala Met Tyr Ser Ser Val
 305 310 315 320
 Asn Lys Pro Gly Gln Leu Val Asn Lys Ser Gly Gln Ser Leu Thr Val
 325 330 335
 Pro Glu Ser Thr Tyr Thr Ser Ile Gln Gly Asp Pro Gln Arg Ser Pro
 340 345 350
 Ser Ser Cys Asn Asp Leu Tyr Ala Thr Val Lys Asp Phe Glu Lys Thr
 355 360 365
 Pro Asn Ser Thr Leu Pro Pro Ala Gly Arg Pro Ser Glu Glu Pro Glu
 370 375 380
 Pro Asp Tyr Glu Ala Ile Gln Thr Leu Asn Arg Glu Glu Glu Lys Ala
 385 390 395 400
 Thr Leu Gly Thr Asn Gly His His Gly Leu Val Pro Lys Glu Asn Asp
 405 410 415
 Tyr Glu Ser Ile Ser Asp Leu Gln Gln Gly Arg Asp Ile Thr Arg Leu
 420 425 430
 <210> 173
 <211> 174
 <212> PRT
 <213> Human

<400> 173

Lys Pro Phe Arg Cys Glu Asn Cys Asn Glu Arg Phe Gln Tyr Lys Tyr
 1 5 10 15

Gln Leu Arg Ser His Met Ser Ile His Ile Gly His Lys Gln Phe Met
 20 25 30

Cys Gln Trp Cys Gly Lys Asp Phe Asn Met Lys Gln Tyr Phe Asp Glu
 35 40 45

His Met Lys Thr His Thr Gly Glu Lys Pro Tyr Ile Cys Glu Ile Cys
 50 55 60

Gly Lys Ser Phe Thr Ser Arg Pro Asn Met Lys Arg His Arg Arg Thr
 65 70 75 80

His Thr Gly Glu Lys Pro Tyr Pro Cys Asp Val Cys Gly Gln Arg Phe
 85 90 95

Arg Phe Ser Asn Met Leu Lys Ala His Lys Glu Lys Cys Phe Arg Val
 100 105 110

Ser His Thr Leu Ala Gly Asp Gly Val Pro Ala Ala Pro Gly Leu Pro
 115 120 125

Pro Thr Gln Pro Gln Ala His Ala Leu Pro Leu Leu Pro Gly Leu Pro
 130 135 140

Gln Thr Leu Pro Pro Pro Pro His Leu Pro Pro Pro Pro Pro Leu Phe
 145 150 155 160

Pro Thr Thr Ala Ser Pro Gly Gly Arg Met Asn Ala Asn Asn
 165 170

<210> 174

<211> 917

<212> PRT

<213> Human

<400> 174

Ala Ser Pro Arg Gly Thr Glu Ala Ser Pro Pro Gln Asn Asn Ser Gly
 1 5 10 15

Ser Ser Ser Pro Val Phe Thr Phe Arg His Pro Leu Leu Ser Ser Gly

20	25	30
Gly Pro Gln Ser Pro Leu Arg Gly Ser Thr Gly Ser Leu Lys Ser Ser		
35	40	45
Pro Ser Met Ser His Met Glu Ala Leu Gly Lys Ala Trp Asn Arg Gln		
50	55	60
Leu Ser Arg Pro Leu Ser Gln Ala Val Ser Phe Ser Thr Pro Phe Gly		
65	70	75
Leu Asp Ser Asp Val Asp Val Val Met Gly Asp Pro Val Leu Leu Arg		
85	90	95
Ser Val Ser Ser Asp Ser Leu Gly Pro Pro Arg Pro Ala Pro Ala Arg		
100	105	110
Thr Pro Thr Gln Pro Pro Pro Glu Pro Gly Asp Leu Pro Thr Ile Glu		
115	120	125
Glu Ala Leu Gln Ile Ile His Ser Ala Glu Pro Arg Leu Leu Pro Asp		
130	135	140
Gly Ala Ala Asp Gly Ser Phe Tyr Leu His Ser Pro Glu Gly Pro Ser		
145	150	155
Lys Pro Ser Leu Ala Ser Pro Tyr Leu Pro Glu Gly Thr Ser Lys Pro		
165	170	175
Leu Ser Asp Arg Pro Thr Lys Ala Pro Val Tyr Met Pro His Pro Glu		
180	185	190
Thr Pro Ser Lys Pro Ser Pro Cys Leu Val Gly Glu Ala Ser Lys Pro		
195	200	205
Pro Ala Pro Ser Glu Gly Ser Pro Lys Ala Val Ala Ser Ser Pro Ala		
210	215	220
Ala Thr Asn Ser Glu Val Lys Met Thr Ser Phe Ala Glu Arg Lys Lys		
225	230	235
Gln Leu Val Lys Ala Glu Ala Glu Ala Gly Ala Gly Ser Pro Thr Ser		
245	250	255

Thr Pro Ala Pro Pro Glu Ala Leu Ser Ser Glu Met Ser Glu Leu Ser
 260 265 270
 Ala Arg Leu Glu Glu Lys Arg Arg Ala Ile Glu Ala Gln Lys Arg Arg
 275 280 285
 Ile Glu Ala Ile Phe Ala Lys His Arg Gln Arg Leu Gly Lys Ser Ala
 290 295 300
 Phe Leu Gln Val Gln Pro Arg Glu Ala Ser Gly Glu Ala Glu Ala Glu
 305 310 315 320
 Ala Glu Glu Ala Asp Ser Gly Pro Val Pro Gly Gly Glu Arg Pro Ala
 325 330 335
 Gly Glu Gly Gln Gly Glu Pro Thr Ser Arg Pro Lys Ala Val Thr Phe
 340 345 350
 Ser Pro Asp Leu Gly Pro Val Pro His Glu Gly Leu Gly Glu Tyr Asn
 355 360 365
 Arg Ala Val Ser Lys Leu Ser Ala Ala Leu Ser Ser Leu Gln Arg Asp
 370 375 380
 Met Gln Arg Leu Thr Asp Gln Gln Gln Arg Leu Leu Ala Pro Pro Glu
 385 390 395 400
 Ala Pro Gly Ser Ala Pro Pro Pro Ala Ala Trp Val Ile Pro Gly Pro
 405 410 415
 Thr Thr Gly Pro Lys Ala Ala Ser Pro Ser Pro Ala Arg Arg Val Pro
 420 425 430
 Ala Thr Arg Arg Ser Pro Gly Pro Gly Pro Ser Gln Ser Pro Arg Ser
 435 440 445
 Pro Lys His Thr Arg Pro Ala Glu Leu Arg Leu Ala Pro Leu Thr Arg
 450 455 460
 Val Leu Thr Pro Pro His Asp Val Asp Ser Leu Pro His Leu Arg Lys
 465 470 475 480
 Phe Ser Pro Ser Gln Val Pro Val Gln Thr Arg Ser Ser Ile Leu Leu
 485 490 495

Ala Glu Glu Thr Pro Pro Glu Glu Pro Ala Ala Arg Pro Gly Leu Ile
500 505 510

Glu Ile Pro Leu Gly Ser Leu Ala Asp Pro Ala Ala Glu Asp Glu Gly
515 520 525

Asp Gly Ser Pro Ala Gly Ala Glu Asp Ser Leu Glu Glu Glu Ala Ser
530 535 540

Ser Glu Gly Glu Pro Arg Val Gly Leu Gly Phe Phe Tyr Lys Asp Glu
545 550 555 560

Asp Lys Pro Glu Asp Glu Met Ala Gln Lys Arg Ala Ser Leu Leu Glu
565 570 575

Arg Gln Gln Arg Arg Ala Glu Glu Ala Arg Arg Arg Lys Gln Trp Gln
580 585 590

Glu Val Glu Lys Glu Gln Arg Arg Glu Glu Ala Ala Arg Leu Ala Gln
595 600 605

Glu Glu Ala Pro Gly Pro Ala Pro Leu Val Ser Ala Val Pro Met Ala
610 615 620

Thr Pro Ala Pro Ala Ala Arg Ala Pro Ala Glu Glu Glu Val Gly Pro
625 630 635 640

Arg Lys Gly Asp Phe Thr Arg Gln Glu Tyr Glu Arg Arg Ala Gln Leu
645 650 655

Lys Leu Met Asp Asp Leu Asp Lys Val Leu Arg Pro Arg Ala Ala Gly
660 665 670

Ser Gly Gly Pro Gly Arg Gly Gly Arg Arg Ala Thr Arg Pro Arg Ser
675 680 685

Gly Cys Cys Asp Asp Ser Ala Leu Ala Arg Ser Pro Ala Arg Gly Leu
690 695 700

Leu Gly Ser Arg Leu Ser Lys Ile Tyr Ser Gln Ser Thr Leu Ser Leu
705 710 715 720

Ser Thr Val Ala Asn Glu Ala His Asn Asn Leu Gly Val Lys Arg Pro
725 730 735

Thr Ser Arg Ala Pro Ser Pro Ser Gly Leu Met Ser Pro Ser Arg Leu
 740 745 750

Pro Gly Ser Arg Glu Arg Asp Trp Glu Asn Gly Ser Asn Ala Ser Ser
 755 760 765

Pro Ala Ser Val Pro Glu Tyr Thr Gly Pro Arg Leu Tyr Lys Glu Pro
 770 775 780

Ser Ala Lys Ser Asn Lys Phe Ile Ile His Asn Ala Leu Ser His Cys
 785 790 795 800

Cys Leu Ala Gly Lys Val Asn Glu Pro Gln Lys Asn Arg Ile Leu Glu
 805 810 815

Glu Ile Glu Lys Ser Lys Ala Asn His Phe Leu Ile Leu Phe Arg Asp
 820 825 830

Ser Ser Cys Gln Phe Arg Ala Leu Tyr Thr Leu Ser Gly Glu Thr Glu
 835 840 845

Glu Leu Ser Arg Leu Ala Gly Tyr Gly Pro Arg Thr Val Thr Pro Ala
 850 855 860

Met Val Glu Gly Ile Tyr Lys Tyr Asn Ser Asp Arg Lys Arg Phe Thr
 865 870 875 880

Gln Ile Pro Ala Lys Thr Met Ser Met Ser Val Asp Ala Phe Thr Ile
 885 890 895

Gln Gly His Leu Trp Gln Gly Lys Lys Pro Thr Thr Pro Lys Lys Gly
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Gly Gly Thr Pro Lys
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<400> 175

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Trp Ser Leu Leu Leu Ala Val Leu Val Phe Phe Leu Phe Ala Leu Pro
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Ser Phe Ile Lys Glu Pro Gln Thr Lys Pro Ser Arg His Gln Arg Thr
 35 40 45

Glu Asn Ile Lys Glu Arg Ser Leu Gln Ser Leu Ala Lys Pro Lys Ser
 50 55 60

Gln Ala Pro Thr Arg Ala Arg Arg Thr Thr Ile Tyr Ala Glu Pro Val
 65 70 75 80

Pro Glu Asn Asn Ala Leu Asn Thr Gln Thr Gln Pro Lys Ala His Thr
 85 90 95

Thr Gly Asp Arg Gly Lys Glu Ala Asn Gln Ala Pro Pro Glu Glu Gln
 100 105 110

Asp Lys Val Pro His Thr Ala Gln Arg Ala Ala Trp Lys Ser Pro Glu
 115 120 125

Lys Glu Lys Thr Met Val Asn Thr Leu Ser Pro Arg Gly Gln Asp Ala
 130 135 140

Gly Met Ala Ser Gly Arg Thr Glu Ala Gln Ser Trp Lys Ser Gln Asp
 145 150 155 160

Thr Lys Thr Thr Gln Gly Asn Gly Gly Gln Thr Arg Lys Leu Thr Ala
 165 170 175

Ser Arg Thr Val Ser Glu Lys His Gln Gly Lys Ala Ala Thr Thr Ala
 180 185 190

Lys Thr Leu Ile Pro Lys Ser Gln His Arg Met Leu Ala Pro Thr Gly
 195 200 205

Ala Val Ser Thr Arg Thr Arg Gln Lys Gly Val Thr Thr Ala Val Ile
 210 215 220

Pro Pro Lys Glu Lys Lys Pro Gln Ala Thr Pro Pro Pro Ala Pro Phe
 225 230 235 240

Gln Ser Pro Thr Thr Gln Arg Asn Gln Arg Leu Lys Ala Ala Asn Phe

	245		250		255
Lys Ser Glu Pro Arg Trp Asp Phe Glu Glu Lys Tyr Ser Phe Glu Ile	260		265		270
Gly Gly Leu Gln Thr Thr Cys Pro Asp Ser Val Lys Ile Lys Ala Ser	275		280		285
Lys Ser Leu Trp Leu Gln Lys Leu Phe Leu Pro Asn Leu Thr Leu Phe	290		295		300
Leu Asp Ser Arg His Phe Asn Gln Ser Glu Trp Asp Arg Leu Glu His	305		310		315
Phe Ala Pro Pro Phe Gly Phe Met Glu Leu Asn Tyr Ser Leu Val Gln	325		330		335
Lys Val Val Thr Arg Phe Pro Pro Val Pro Gln Gln Gln Leu Leu Leu	340		345		350
Ala Ser Leu Pro Ala Gly Ser Leu Arg Cys Ile Thr Cys Ala Val Val	355		360		365
Gly Asn Gly Gly Ile Leu Asn Asn Ser His Met Gly Gln Glu Ile Asp	370		375		380
Ser His Asp Tyr Val Phe Arg Leu Ser Gly Ala Leu Ile Lys Gly Tyr	385		390		395
Glu Gln Asp Val Gly Thr Arg Thr Ser Phe Tyr Gly Phe Thr Ala Phe	405		410		415
Ser Leu Thr Gln Ser Leu Leu Ile Leu Gly Asn Arg Gly Phe Lys Asn	420		425		430
Val Pro Leu Gly Lys Asp Val Arg Tyr Leu His Phe Leu Glu Gly Thr	435		440		445
Arg Asp Tyr Glu Trp Leu Glu Ala Leu Leu Met Asn Gln Thr Val Met	450		455		460
Ser Lys Asn Leu Phe Trp Phe Arg His Arg Pro Gln Glu Ala Phe Arg	465		470		475
					480

Glu Ala Leu His Met Asp Arg Tyr Leu Leu Leu His Pro Asp Phe Leu
 485 490 495

Arg Tyr Met Lys Asn Arg Phe Leu Arg Ser Lys Thr Leu Asp Gly Ala
 500 505 510

His Trp Arg Ile Tyr Arg Pro Thr Thr Gly Ala Leu Leu Leu Leu Thr
 515 520 525

Ala Leu Gln Leu Cys Asp Gln Val Ser Ala Tyr Gly Phe Ile Thr Glu
 530 535 540

Gly His Glu Arg Phe Ser Asp His Tyr Tyr Asp Thr Ser Trp Lys Arg
 545 550 555 560

Leu Ile Phe Tyr Ile Asn His Asp Phe Lys Leu Glu Arg Glu Val Trp
 565 570 575

Lys Arg Leu His Asp Glu Gly Ile Ile Arg Leu Tyr Gln Arg Pro Gly
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Pro Gly Thr Ala Lys Ala Lys Asn
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<400> 176

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Leu Thr His Ser Trp Glu Ile Gln Leu Leu Leu Leu Val Phe Ser Ser
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Val Leu Tyr Val Ala Ser Ile Thr Gly Asn Ile Leu Ile Val Phe Ser
 35 40 45

Val Thr Thr Asp Pro His Leu His Ser Pro Met Tyr Phe Leu Leu Ala
 50 55 60

Ser Leu Ser Phe Ile Asp Leu Gly Ala Cys Ser Val Thr Ser Pro Lys
 65 70 75 80

Met Ile Tyr Asp Leu Phe Arg Lys Arg Lys Val Ile Ser Phe Gly Gly
85 90 95

Cys Ile Ala Gln Ile Phe Phe Ile His Val Ile Gly Gly Val Glu Met
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Val Leu Leu Ile Ala Met Ala Phe Asp Arg Tyr Val Ala Leu Cys Lys
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Pro Leu His Tyr Leu Thr Ile Met Ser Pro Arg Met Cys Leu Ser Phe
130 135 140

Leu Ala Val Ala Trp Thr Leu Gly Val Ser His Ser Leu Phe Gln Leu
145 150 155 160

Ala Phe Leu Val Asn Leu Ala Phe Cys Gly Pro Asn Val Leu Asp Ser
165 170 175

Phe Tyr Cys Asp Leu Pro Arg Leu Leu Arg Leu Ala Cys Thr Asp Thr
180 185 190

Tyr Arg Leu Gln Phe Met Val Thr Val Asn Ser Gly Phe Ile Cys Val
195 200 205

Gly Thr Phe Phe Ile Leu Leu Ile Ser Tyr Val Phe Ile Leu Phe Thr
210 215 220

Val Trp Lys His Ser Ser Gly Gly Ser Ser Lys Ala Leu Ser Thr Leu
225 230 235 240

Ser Ala His Ser Thr Val Val Leu Leu Phe Phe Gly Pro Pro Met Phe
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Val Tyr Thr Arg Pro His Pro Asn Ser Gln Met Asp Lys Phe Leu Ala
260 265 270

Ile Phe Asp Ala Val Leu Thr Pro Phe Leu Asn Pro Val Val Tyr Thr
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 35 40 45

Ala Glu Ala Lys Val Lys Ala Leu Lys Ala Lys Lys Ala Val Leu Lys
 50 55 60

Gly Val Arg Ser His Thr Gln Lys Arg Arg Ser Ala Cys His Ser Pro
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Ser Gly Gly Pro Arg His Cys Asp Ser Gly Gly Ser Pro Asp Ile Leu
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Phe Arg

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Leu Glu Asn Ile Ser His Leu Val Ser Ile Gly Glu Asp Phe Thr Gln
 35 40 45

His Ile Ala Leu Thr Gln Asn Val Ile Thr Tyr Met Arg Thr Lys His
 50 55 60

Phe Val Ser Lys Lys Phe Gly Lys Ile Phe Ser Asp Trp Leu Ser Phe
 65 70 75 80

Asn Gln His Lys Glu Ile His Thr Lys Cys Lys Ser Tyr Gly Ser His
 85 90 95

Leu Phe Asp Tyr Ala Phe Ile Gln Asn Ser Ala Leu Arg Pro His Ser
 100 105 110

Val Thr His Thr Arg Glu Ile Thr Leu Glu Cys Arg Val Cys Gly Lys
 115 120 125

Thr Phe Ser Lys Asn Ser Asn Leu Arg Arg His Glu Met Ile His Thr
 130 135 140

Gly Glu Lys Pro His Gly Cys His Leu Cys Gly Lys Ala Phe Thr His
 145 150 155 160

Cys Ser Asp Leu Arg Lys His Glu Arg Thr His Thr Gly Glu Lys Pro
 165 170 175

Tyr Gly Cys His Leu Cys Gly Lys Ala Phe Ser Lys Ser Ser Asn Leu
 180 185 190

Arg Arg His Glu Met Ile His Thr Arg Glu Lys Ala Gln Ile Cys His
 195 200 205

Leu Cys Gly Lys Ala Phe Thr His Cys Ser Asp Leu Arg Lys His Glu
 210 215 220

Arg Thr His Leu Gly Asp Lys Pro Tyr Gly Cys Leu Leu Cys Gly Lys
 225 230 235 240

Ala Phe Ser Lys Cys Ser Tyr Leu Arg Gln His Glu Arg Thr His Asn
 245 250 255

Gly Glu Lys Pro Tyr Glu Cys His Leu Cys Gly Lys Ala Phe Ser His
 260 265 270

Cys Ser His Leu Arg Gln His Glu Arg Ser His Asn Gly Glu Lys Pro
 275 280 285

His Gly Cys His Leu Cys Gly Lys Ala Phe Thr Glu Ser Ser Val Leu
 290 295 300

Lys Arg His Glu Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys His
 305 310 315 320

Val Cys Gly Lys Ala Phe Thr Glu Ser Ser Asp Leu Arg Arg His Glu
 325 330 335

Arg Thr His Thr Gly Glu Lys Pro Tyr Glu Cys His Leu Cys Gly Lys
 340 345 350

Ala Phe Asn His Ser Ser Val Leu Arg Arg His Glu Arg Thr His Thr
 355 360 365

Gly Glu Lys Pro Tyr Glu Cys Asn Ile Cys Gly Lys Ala Phe Asn Arg
 370 375 380

Ser Tyr Asn Phe Arg Leu His Arg Arg Val His Thr Gly Glu Lys Pro
 385 390 395 400

Tyr Val Cys Pro Leu Cys Gly Lys Ala Phe Ser Lys Phe Phe Asn Leu
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Arg Gln His Glu Arg Thr His Thr Lys Lys Ala Met Asn Met
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 <213> Murine

<400> 179
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 <213> Murine

<400> 180

Asn Tyr Gly Val His
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<210> 181
 <211> 48

<212> DNA
<213> Murine

<400> 181
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48

<210> 182
<211> 16
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<400> 182

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<210> 183
<211> 33
<212> DNA
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gccctcacct actatgatta cgagtttgct tac

33

<210> 184
<211> 11
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<400> 184

Ala Leu Thr Tyr Tyr Asp Tyr Glu Phe Ala Tyr
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agggccagtc agagtattgg cacaacata cac

33

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<400> 186

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<210> 187

<211> 18
<212> DNA
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<400> 187
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18

<210> 188
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<400> 188

Ala Ser Glu Ser Ile Ser
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<210> 189
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<212> DNA
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caacaaaata ataactggcc aaccacg

27

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Gln Gln Asn Asn Asn Trp Pro Thr Thr
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17

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gtgaccaggc gcccaatac

19

<210> 193
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<400> 193
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19

<210> 194
<211> 21
<212> DNA
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<220>
<223> EGFR oligonucleotide

<400> 194
agccgaggca gggaatgcgt g

21

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- (74) Agents: **GOLIAN, Paul, D. et al.**; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, New Jersey 08543-4000 (US).
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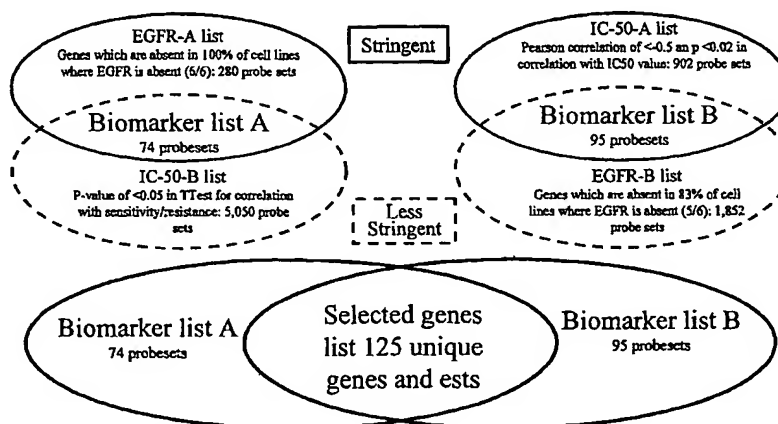
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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM,

[Continued on next page]

- (54) Title: **BIOMARKERS AND METHODS FOR DETERMINING SENSITIVITY TO EPIDERMAL GROWTH FACTOR RECEPTOR MODULATORS**



- (57) Abstract: EGFR biomarkers useful in a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises (a) exposing the mammal to the EGFR modulator and (b) measuring in the mammal level of at least one biomarker, wherein a difference in the level in at least one biomarker measured in (b) compared to the level of the biomarker in a mammal that has not been exposed to the EGFR modulator indicates that the mammal will respond therapeutically to the method of treating cancer.



ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,

BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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